APR 23 1929

**Give Me a Due and Decent Esteem of My Profession and of Myself, That I May Regard No Man's Occupation Higher Than Mine, Envying None so Long as I Serve Honorably and Well the Sick and the Injured.**—*Paraphrased.*

Vol. XVIII, No. 4 APRIL, 1929

# JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 77th ANNUAL MEETING WILL BE HELD AT RAPID CITY (BLACK HILLS), SOUTH DAKOTA, DURING WEEK OF AUGUST 26, 1929.

F. W. Brown, Lead, So. Dak., Local Secretary

The 1929 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conferences of Pharmaceutical Association Secretaries will also be held at Rapid City, same time and place.

For Association Roster and Roster of the Boards of Pharmacy, of Officers of Pharmaceutical Associations, Local Branches, see pages x, xii, xiv, etc.

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# TIME.

TIME, it seems, is the universal balance-wheel. It has no bonds, except those which we arbitrarily impose upon it. It is not ruled, in its whirl through space, by clock or whistle, nor years, nor life, nor death.

*"—You will sometimes catch, if you listen long,*
*A song of a million years."*

The Bad Lands of South Dakota bear a testimony, mute, yet voluminous, of the great, slow, forward tidal surge of Time,

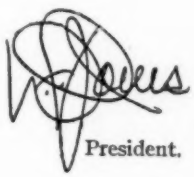
*"—Traced in the score of the strata marks.*
*"While millenniums winked like campfire sparks*
*Down the winds of unguessed time."*

Time too, has had its part to play in the evolution of pharmacy as we know it to-day, and the strata marks are graved as immutably upon the pages of history as are those æons upon the outcroppings of the Bad Lands.

LaWall places Pharmacy's age at four thousand years. During that time, from a crude beginning has sprung a great and varied profession, possessed of a knowledge of the greatest of all arts—the molding of Destiny as it touches upon human welfare.

There have been many side issues, and to-day we find among us those who have nearly lost sight of that hallowed Cause to which they once gave allegiance, beneath the visional obstructions with which they have surrounded themselves in their haste for gain.

Though stray we may, Time still grinds fine in its mill of years, and the "run is true to color."



President.

Watertown, S. D., April 1929.

FLOYD W. BROWN.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XVIII APRIL, 1929 No. 4

## FLOYD W. BROWN.

Floyd W. Brown, of Lead, who enjoys the unusual distinction of holding both the office of Local Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION and President of the South Dakota Pharmaceutical Association, was born in 1876 on a farm in Illinois near the city of Galesburg. At an early age he left home and started out for himself; in 1890 he secured a position in the drug store of Emil Brauch at Hurley, South Dakota; soon after, he moved to Sioux City, Iowa, where he remained until 1896.

In 1896, Mr. Brown returned to South Dakota and entered the employment of W. R. Dickenson, owner of the Dickenson Drug Company of Lead. This move was the beginning of an active career in pharmacy and politics of South Dakota.

In 1897 Mr. Brown wrote the examinations of the State Board of Pharmacy and received some very high grades. In 1900, he started in business for himself in Lead at 4 Main Street; in 1904, be bought the stationery store next door, on the corner, and moved into that building, his present location.

Mr. Brown early in his career elected to increase his lines and introduce a merchandising system in addition to his prescription trade, and when he took over the corner location he at once put his merchandising methods into effect. Coming to the conclusion that methods which had been productive of good results in Lead would prove successful elsewhere, he, in 1919, purchased a drug store in Belle Fourche in which the same policies of merchandising were carried out. Again meeting with success in this venture he, in 1924, purchased a store in Deadwood.

Miss Elizabeth Brown, a daughter, will receive the Bachelor of Science degree from the Philadelphia College of Pharmacy and Science, this year. Mr. Brown's son is engaged with his father in the stores.

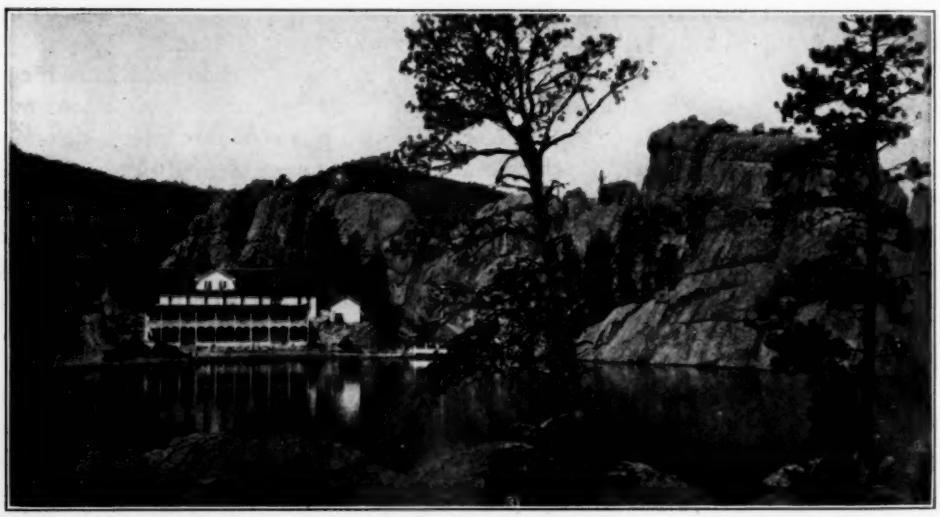
Mr. Brown's organization shows some interesting data on labor turnover and self-trained employees. The manager of the Belle Fourche Store is John E. Dignan, who has been in Mr. Brown's employ for eighteen years. Frank Wilson, the manager of the Deadwood store, has been with him nine years. Mrs. Francys Lewis Green, who is account clerk for all three stores, is finishing her sixth

year. A. W. Powell and Joel Rasmusson, of the Belle Fourche and Deadwood stores, respectively, have both worked for Mr. Brown three years. Frank Teskey has been with Mr. Brown two years, coming from Crookston, Minnesota, to take charge of the Lead store. These are all good service records and the longer ones are exceptional. The subject of this brief sketch claims the reason for his unusually small labor turnover is due to the care with which he picks his men. There is another quality—ability to command loyalty.

Mr. Brown's ability has been extended, not only in his private business, but to wider fields. In 1910, he was appointed to the State Board of Pharmacy; he remained on this Board until 1917, giving freely of his time and ability. In 1917 he was appointed to the state Board of Charities and Corrections and served on the Board as Secretary for five years. A lasting monument to human health was established during his office, in the South Dakota State Tubercular Sanitarium, for which much credit is due him.

Mr. Brown is a staunch booster and an ardent lover of the beautiful Black Hills, which form the setting of both his home and business fields. Through his efforts, the druggists of the Black Hills—West River Territory have formed a local organization, which is very active in looking after the welfare of their common interests, and promoting general interest in the "Wonderland of America."

At the annual convention last August, at Huron, Mr. Brown was elected President of the South Dakota Pharmaceutical Association. Following closely upon this honor came the appointment as Local Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION for the ensuing year, and he is now busily organizing and executing the plans for the entertainment of the body's seventy-seventh annual meeting, which will convene at Rapid City during the week of August 26, 1929. In these offices, Mr. Brown's executive ability again comes into play, both for the benefit of his state association and also in the service of Pharmacy's great national organization.—Data for article contributed by G. A. BENDER.



Sylvan Lake—Beautiful little rock-bound, ice-cold lake high among the peaks of Mount Harney.

# EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase St., BALTIMORE, MD.

## IN SERVICE.

THE deaths, within a few weeks, of the secretaries of the pharmaceutical associations of two adjoining states is an unusual and disturbing occurrence. The deaths of Secretary Churchill of the Vermont Association and Secretary Guerin of the Massachusetts Association are of national as well as local importance and regret to Pharmacy, since they mark the passing of two able officials who have served their associations not only efficiently but also for such a length of time as to be connecting links between the past and the present.

These two gentlemen were pharmacists with high ideals and practical viewpoints, who put into every-day application the principles for which they stood, who commanded the respect and support to a remarkable extent of their fellow-pharmacists, and who combine to an unusual degree, the optimism and progressiveness of youth with the sound conservatism of age and experience. They were able to and did exert a great influence upon the development of pharmacy of their respective states and indirectly of the country at large.

Some day a pharmaceutical historian will record the unselfish and effective services which the state pharmaceutical association secretaries have rendered to their profession, to their fellow-pharmacists and to the public. It is not a position of glory but rather of exacting requirement and hard work. The very length of service of the devoted men who have, in the great majority of cases, been *called* to these positions since the state associations have been in existence, bears ample witness to the fact that they have rendered acceptable service and won the approval and affection of those for whom they have worked.

Secretary Churchill and Secretary Guerin have won a place among the most distinguished of the state association secretaries by the quality as well as length of their service and they will be sorely missed.

---

## THE ARCHITECT OF THE HEADQUARTERS BUILDING.

THE selection of Mr. John Russell Pope, of New York City, to design and supervise the construction of the Headquarters Building, as announced elsewhere in this issue, is an assurance that the progress so far made in the enterprise justifies the taking of this important step and that a building will be erected which will be a credit to the profession of pharmacy and to the really wonderful location in which it is to be situated.

Mr. Pope is one of the outstanding architects of this country and his work bears witness to the fact that he has the rare gift of combining beauty of design with usefulness. The Headquarters Building should be both monumental and serviceable.

The Commission of Fine Arts report that more than a million persons visit the Lincoln Memorial annually and no estimate can be made of the number that are not recorded. The Arlington Memorial Bridge over the Potomac will be the gateway to and from the South and Southwest. The location of the Headquarters

Building will of necessity bring it to the attention of this constantly increasing number of visitors from every section of the country and many of them from foreign lands. How important it is, then, that the Building should impress them with the importance of Pharmacy and of the value of the service which it renders in connection with the public health.

At the same time, the institution must render the service which can be rightfully expected from it by the thousands of pharmacists of the country and especially by those who contributed to it and thereby made it possible. It must become to the greatest possible extent, a "service station," as it has been expressed; for the Headquarters Building will provide, for the first time in the history of American Pharmacy, the opportunity and equipment for real coöperative efforts in education, in legislation, in research, in commerce and in publicity.

The correspondence with Mr. Pope and the preliminary designs which he has prepared demonstrate that he fully appreciates both of these needs and that they can be worked out satisfactorily.

American Pharmacy is just now facing some adjustments which are challenging to its future progress. It is indeed encouraging that such satisfactory progress can be reported in the Headquarters Building project, that such a valuable site is ours, that we have the sympathetic and helpful interest of the Commission of Fine Arts and the Parks and Planning Commission, and that we are to have the assistance and guidance of such an architect as Mr. Pope in translating our dreams into a reality.

---

## COÖPERATIVE SERVICE.

RECENTLY, a speaker stated, in substance, that "team work" instills a spirit of emulation, eliminates sloth and imposes an accountability which is essential to every type of human endeavor; provided, that applicability and practicability receive due consideration. We quote a petition from Dr. Frank Crane "The Prayer of the Physician," which may easily be paraphrased for the pharmacist: "Give me a due and decent self-esteem, that I may regard no man's occupation higher than mine, envying not the king upon his throne so long as I am prime minister to the suffering."

Not very long ago *Hygeia* carried the following message to the public, which embodies the spirit of "team work." It is told in words the layman can understand and instills in him confidence in the physician and pharmacist.

### "I UNDERSTAND HOW SERIOUS IT IS."

"There is serious sickness at home, and you hurry with the prescription the Doctor has given you to your local prescription pharmacy. The Pharmacist immediately senses the seriousness of the case from the medicine the Doctor has ordered. Every minute that treatment is delayed counts against the patient.

"A fraction of a grain of some powerful medicament enters into the prescription—perhaps a rare drug or a new remedy. Yes, the Pharmacist assures himself, he has every ingredient—he must be prepared for emergencies. Cooly, deftly, accurately, he compounds the prescription, and carefully checks his work.

"As you hurry from the pharmacy with the medicine, does it occur to you that your prescription pharmacy is entitled to a generous measure of support from the people of the neighborhood? There isn't enough prescription business in most communities to support an exclusively prescription drug store. Therefore the druggist must sell many sundries—he must be a mer-

chant, too. Only by doing this can he make a living, and maintain his pharmacy, in equipment and efficiency, so that it may best serve the needs of the community and its physicians when serious sickness comes."

---

## APPLICABLE KNOWLEDGE.

Underlying professional attainments there must be adequate education. The pharmacist needs not only experience but a knowledge which enables him to understand what he sees and does. At the formal opening of Johns Hopkins (1876) Thomas H. Huxley delivered an address on "University Education." We are taking the liberty of quoting the following which applies to medical and pharmaceutical education:

". . . Again, Materia Medica, so far as it is a knowledge of drugs, is the business of the druggist. In all other callings the necessity of the division of labor is fully recognized, and it is absurd to require of the medical man that he should avail himself of the special knowledge of those whose business it is to deal in the drugs which he uses. . . . "

"All knowledge is good. It is impossible to say that any fragment of knowledge, however insignificant or remote from one's ordinary pursuits, may not some day be turned to account. But in medical education, above all things, it is to be recollected that, in order to know a little well, one must be content to be ignorant of a great deal."

---

## ESSENTIALS OF A REGISTERED HOSPITAL.

THE issue of the *Journal of the American Medical Association* for March 30th is largely devoted to hospital service and is, therefore, of interest to pharmacists. The AMERICAN PHARMACEUTICAL ASSOCIATION is affiliated with the American Conference on Hospital Service. The following is quoted from the *Jour. A. M. A.:*

"In its work with hospitals it is the desire of the Council on Medical Education and Hospitals to coöperate in every way possible for the improvement of hospital service, whereby sick or injured people may be provided with the best possible care. The Council does not claim to have, nor does it assume any legal authority over any hospital, but recognizes clearly that the officers in charge of such institutions have the unquestioned right to conduct the hospitals in any way they deem wise. If a hospital desires to have the Council's endorsement, however, and that is what the Council's approval actually means, it should not be unwilling to comply with the principles which the Council deems necessary for such endorsement. The following essentials, or principles have been prepared by the Council with the sole intention and desire of dealing with equal fairness to all institutions. A hospital seeking admission to the Register, therefore, should have the following qualifications:

"1. A staff made up of one or more properly qualified physicians who shall be graduates of reputable medical schools; and all physicians treating patients in the hospital must be so qualified.

"2. An able management which, depending on the size of the hospital may be in the hands of a competent physician, an able superintendent, or a board of trustees.

"3. A competent physician-pathologist, either on the staff or easily accessible, who

should examine and keep a careful record of tissues removed at all operations conducted in the hospital.

"4. Careful histories and records of all patients admitted to the hospital with which should be filed reports of any laboratory analyses, roentgen-ray findings or pathologic reports of any tissues examined.

"5. One or more competent nurses depending on the average number of its patients.

"6. Regular staff conferences, at least monthly and preferably weekly, in all hospitals having staffs of three or more physicians. At these staff conferences complicated cases in the hospital should be considered, as well as all deaths occurring in the hospital during the period intervening between meetings. If necropsies have been held on any of these patients, these especially should be given discussion in which antemortem and postmortem signs, symptoms and observations should be compared.

"7. Hospitals are institutions which should not be conducted for profit but for the purpose of securing better medical service for the community and they should always be conducted in accordance with the code of ethics of the American Medical Association."

It would seem that the pharmacist should have recognition in the qualifications mentioned above, in fact, the staff of every hospital should include a pharmacist, qualified by education and training.

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## A BROADER FIELD OF ACTIVITY IN THE AIMS AND PURPOSES OF A. PH. A. BRANCHES.

THE Northern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was reorganized in the fall of 1928 on an entirely new plan with the hope that it would become more successful than it has been in the past.

It had been reorganized a number of times and conducted upon the same plan as the other branches; it functioned for a time and then demised.

This time it was decided to try out a new plan that might add more interest and bring together those men in pharmacy particularly interested in its professional side. To that end a Constitution and By-Laws were adapted from those of the The Academy of Medicine of Cleveland. Under this Constitution a Council of sixteen members was chosen who meet monthly in the evening at 6 P.M. dinner. This meeting must and always has adjourned not later than 7:30 P.M. No less than thirteen members have been present at each Council meeting. All the business of the organization is conducted by the Council, and the membership at large elects the Council. Membership is selective; prospective members may apply. Their applications are referred to a membership committee who investigate the applicants and their stores and make recommendations to the Council. The Council elects or rejects the applicants; no one is urged to become a member, but anyone who meets the requirements of the A. PH. A. is eligible to apply for membership.

The Branch has met as a Council each month during the winter and has held one General Branch meeting open to all the druggists, physicians and research workers of the city, when the attendance was seventy-six. It is proposed to hold one more such meeting this month and, later, one for druggists only. The Council will have a dozen or more applications for membership to be acted upon at its next meeting.

The real purpose of the organization is to advance pharmacy and a definite plan is in mind to do so. This plan is one of quiet work, which is properly mapped out, to interest physicians in real pharmaceutical service and to prove to them

that it is really obtainable. The organization is doing nothing sporadic or spectacular but thus far its work has shown actual results. It is the desire of the Branch to publish just how it does it and what it accomplishes, as soon as it has more records of accomplishment behind it.

The Branch operates on the theory that no one wants to join anything he is urged to join, but all want to be in and help to success an organization that is succeeding and does not solicit membership. The Constitution and By-Laws are published in the Department for Local Branches of this issue of the JOURNAL and the Branch invites criticism and suggestions.

It is not beyond reason to predict that some day there may come such an increase in A. PH. A. membership that only names submitted by the Branch will be taken into the A. PH. A. from this district. What could build a better AMERICAN PHARMACEUTICAL ASSOCIATION? With a number of such branches in existence it would then be possible to provide for visits from the General Secretary and other officers that would be an aid and an inspiration to professional pharmacy.—EDWARD SPEASE.

---

## NOTE FROM THE A. PH. A. COMMITTEE ON TRANSPORTATION.

T. J. BRADLEY, CHAIRMAN.

Since the list of reduced rates to the 1929 meeting of the ASSOCIATION at Rapid City, South Dakota, was published in the January number of the JOURNAL, the western railroads have announced summer excursion rates from California and other western states, at a substantial reduction from regular fares. We have been unable to secure the exact rates as yet, but members can find out what they are by inquiring at their railroad ticket offices.

Switchback on the Needles Road—Hairpin Turn, with cathedral spires in the background.

# SCIENTIFIC SECTION

## DIFFERENTIAL CHARACTERS OF THREE COMMON CHINESE SPECIES OF EPHEDRA.

BY J. C. LIU AND B. E. READ.*

Received for publication, December 18, 1928.

In a previous communication to THIS JOURNAL (3), upon the botanical sources of ephedrine and pseudoephedrine, the botanical characteristics of *Ephedra sinica*, Stapf and *E. equisetina*, Bge. were described, and we stated that "the material collected and sold as Mahuang consists chiefly of *Ephedra sinica*, Stapf." This is true for the north of China, to which our investigations hitherto have been confined. Conditions have now enabled us to investigate the Central China markets and we find a third species of Ephedra, *Ephedra distachya*, L., that is collected and sold in that area. This is a well-known plant, the botanical description of which can be found in authoritative books. It was collected in Shansi by Smith (5), and we have many samples from the Hankow market, and the mountain areas west of Chihli, which assure us that this species is important and probably is the chief source of supply of Mahuang for Central China.

Seeing that the drug Mahuang appears upon the market without flowers, fruit or leaves (excepting bracts), we are presenting the chief points of differences in these three species of Ephedra, so that their pharmacognostic character may be readily observed and the necessary distinctions be made.

If the drug appears complete with its main stems and roots, gross inspection will be sufficient to indicate which of the species has been collected.

More often incomplete plants are available; just the stems or chopped stems are used, having been freed from the useless roots and woody material. These stems may be complete enough to readily indicate their origin by the length of their internodes, by the roughness of their surfaces and by the degree of roundness, but more often one finds the material so finely chopped that a short histological study is necessary. We herewith give the chief points of difference with simple stains.

A good deal of Mahuang is sold at the ports in powder form. A microscopic study may be helpful in showing the large number of wood cells present in *E. equisetina;* subsequently a few simple chemical tests give the desired distinctions. Complete chemical analyses are being undertaken in these laboratories, a report of which will be published separately; simple ash determinations are here given for diagnostic purposes.

Commercially the present relative importance of the three species probably stands in the following order, *E. sinica*, *E. distachya* and *E. equisetina*. In 1885 the Customs returns show that Mahuang was exported in quantity from the following places: Newchwang 966 piculs, Tientsin 213 piculs, Hankow 66 piculs, Ningpo 61 piculs. Newchwang and Tientsin material would be chiefly *Ephedra sinica*, Hankow and Ningpo would be *Ephedra distachya*, about a tenth of the total. This is

* Department of Pharmacology, Peking Union Medical College, Peking, China.

not to say that *E. equisetina* is scarce; there is much of it, and with the great demand during the last few years much of it has been collected, which freed from the woody stems we have shown has an unusually high content of ephedrine. *E. distachya* we have analyzed and found similar to *E. sinica* in containing both ephedrine and pseudoephedrine in the proportion of about four to one, but the total alkaloid we found to be less than *Ephedra sinica* by about 30 per cent.

The large export of Mahuang from Tientsin during the past three years has been reported upon in detail (4). With the disturbed conditions prevailing it is impossible to say how this would be in normal times. To offset the difficulties encountered with shipping at Tientsin there has been systematic collection of the wild plant by the International Famine Relief Association at Tatungfu, North Shansi, so that the supply has been well kept up. In Central China railway and shipping facilities are improving and supplies may pass down the Yangtse, in which case larger amounts of *E. distachya* are likely to appear on the market.

## I. GROSS STRUCTURE.

The appearance of the flowers and fruits are quite characteristic for the species examined, which would be the natural basis for differentiation botanically. However, the drug is collected after the flowering and fruiting season and we have scarcely ever seen a single fruit or flower in twenty-five tons of the drug coming from various places. Special collections made by us or for us at other seasons of the year may bear flowers or fruit, but the latter is so easily shaken off it is hard to transport intact specimens.

Hence a macroscopic study of the drug is limited to an examination of the whole plant for size and habit, the stems and the minute leaves. We have drawn up in Table I the differential characteristics of these three species of Ephedra, and from it one can readily pick out the essential differences in length of internode, surface of stem, shape of stem and appearance of the leaf; see Table V.

TABLE I.—MACROSCOPIC STUDIES OF THREE CHINESE EPHEDRAS.

| | *E. sinica.* | *E. distachya.* | *E. equisetina.* |
|---|---|---|---|
| (1) Habit | (*a*) Herbaceous<br>(*b*) Not branching (or only occasionally so near base) | (*a*) Slightly woody<br>(*b*) Branching, from upper and lower parts of main stem | (*a*) Very woody<br>(*b*) Very much branching |
| (2) Stems | | | |
| (*a*) Length | About 30 cm. | About 37 cm. | 1/4 to 2 meters |
| (*b*) Color (when dried) | Ashy greyish green | Greenish yellow (not ashy) | Ashy yellowish green |
| (*c*) Surface | Slightly rough | Rough | Very smooth |
| (*d*) Shape | Ancipital (flat) | Roundish round | Round |
| (*e*) Thickness | Broad 1.5 to 2.1 mm., thick 1.07 to 1.13 mm. | 1.6 to 2.1 mm. | 1.27 to 1.55 mm. |
| (3) Internodes | | | |
| (*a*) Length | 3 to 6 cm. | 2.5 to 6 cm. | 1 to 2.5 cm. |
| (*b*) Average length | 3.54 cm. | 3.27 cm. | 1.92 cm. |
| (*c*) Average weight | 21.3 Gm. | 27.2 Gm. | 13.1 cm. |
| (4) Leaves (all minute) | | | |
| (*a*) Length | 4 mm. | Similar to E. sinica | 2 mm. |
| (*b*) Color | Reddish brown base, white lamina | | Brownish purple, lamina dark |
| (*c*) Position | Tips subulate, recurved | Often fissioned at base | Close to stem |

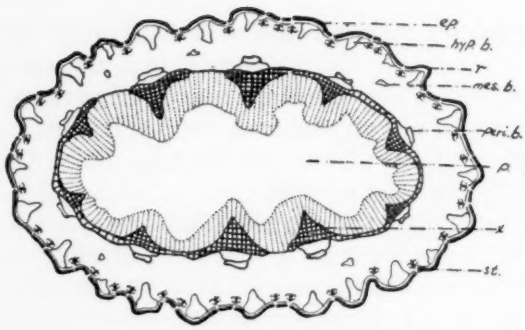


Fig. 1.—Ephedra sinica, Stapf.

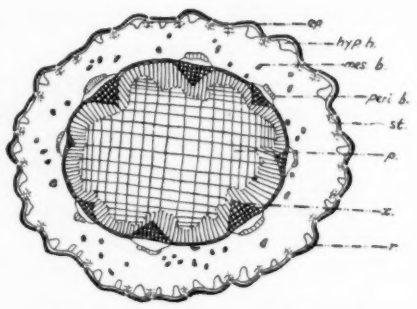


Fig. 3.—Ephedra equisetina, Bge.

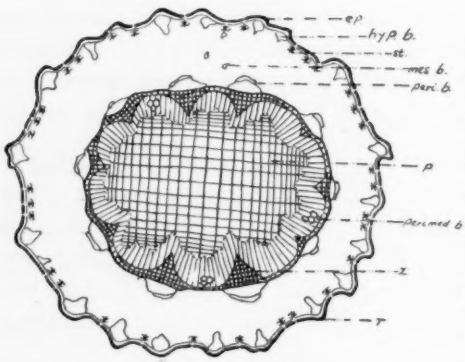


Fig. 2.—Ephedra distachya, L.

Figs. 1, 2 and 3.—Camera lucida pictures of cross-sections of 3 Chinese Ephedras, showing (1) the general round or flattish shape (2) the angulate or undulate outline; and (3) the lignification, represented by heavy straight lines. *ep.*, epidermis; *hyp. b.*, hypodermal basts; *mes. b.*, mesocortical basts; *peri. b.*, pericyclic basts; *perimed. b.*, perimedullary basts; *p.*, pith; *x.*, xylem; *st.*, stomata; *r.*, ridges.

Fig. 1.—In *E. sinica*, neither pith nor any bast is lignified, perimedullary absent, and mesocortical basts few or absent.

Fig. 2.—In *E. distachya*, pith and perimedullary basts present and lignified; mesocortical basts present or absent.

Fig. 3.—In *E. equisetina*, pith and all, except hypodermal basts, lignified; perimedullary absent, and mesocortical basts numerous.

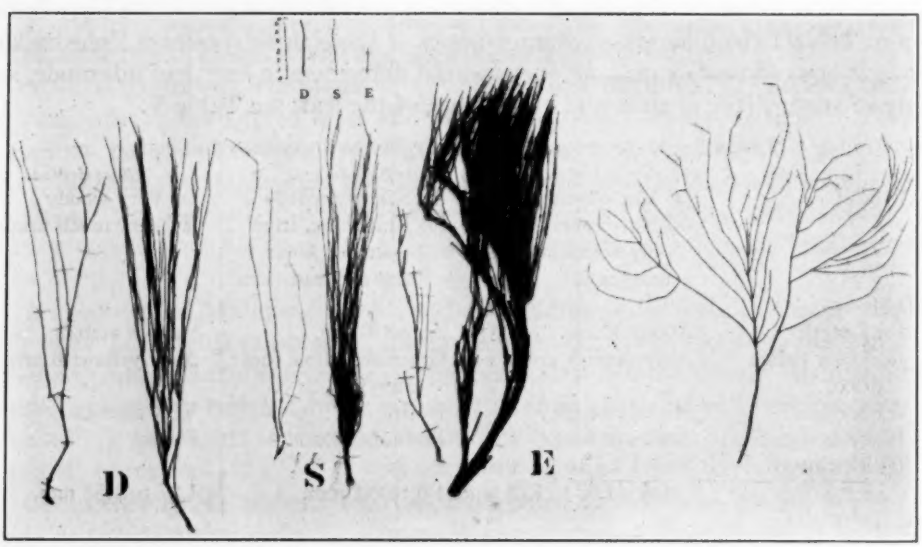


Fig. 4. Fig. 5.

Fig. 4.—Gross appearance of the three common Chinese species of Ephedra. D, *Ephedra distachya*, L. (notice the branching); S, *E. sinica*, Stapf (notice the simple habit and the recurved tip of leaf); E, *E. equisetina*, Bunge, upper part of plant (notice the branching; the woody stem; the short internode and the tiny leaves). D and S complete plant.

Fig. 5.—*Ephedra distachya*, L. (spread out to show branching). Cultivated in the garden of the Peking Union Medical College.

## II. HISTOLOGICAL STRUCTURES.

*A. Brief History.*—Efforts to identify the species of Ephedra through histological means have been attempted by various botanists. The result, so far, has not been satisfactory. In his monograph on Ephedra (6), Dr. Stapf in 1889 made the following summary of the situation up to that time. "Details of the anatomical structure of the stem of Ephedras are scattered in a great number of special treatises and bulletins, notably in De Bary's "Comparative Anatomy of the Phanerogams and Ferns." Bertrand (1) gave a very clear description of the same. In conclusion, Bertrand says that "the anatomical structures of the different species suggest only quite insufficient and unreliable characteristics for classification. In view of the large amount of research material at my disposal, I believed that the matter might be undertaken afresh. The final conclusion was, however, the same."

Graham (2) in 1907 took the number of vascular bundles in the second internode from the apical bud, and the presence or absence of different tissues and cell contents in some 16 species of Ephedra, for the purpose of classification. Although we agree with him that the number of vascular bundles in the second internode, from the apex, of *E. distachya* is constant, namely 8, such fortunate regularity does not exist, however, in the other two oriental species, *E. sinica* and *E. equisetina* Bge., which Graham did not examine, as seen from the following tables. Again after the plant has been collected inland, dried, packed and shipped frequently from one side of the globe to the other, it is impossible to decide with certainty whether the second internode on the crude drug is actually the second internode from the apical bud.

*B. Method for Differentiating Three Chinese Ephedra Species Based on Lignification.*—The histology of Ephedra has been given by Graham (2) and other authorities (6). In this article we are not concerned with the details of the structures, except the pith and the four groups of basts or stereoms; namely, the hypodermal, the mesocortical (intercortical), the pericyclic and the perimedullary, named in their order of occurrence from the periphery to the center. In applying one or two drops each of phloroglucin and concentrated hydrochloric acid to cross-sections of Ephedra which can be made easily by free-hand cutting, the lignified tissues will be stained red, while cellulose cells remain unchanged. It was observed that some of the tissues mentioned above are lignified differently in the three species of Ephedra in question. Incorporating this feature with a few other simple observations, the three species of Ephedra can be easily differentiated. The results of our observations are drawn up in Tables II, III and IV, and are given in detail in Figs. 1, 2 and 3.

TABLE II.—MICROSCOPIC STUDIES OF *Ephedra sinica*, STAPF.

| Number of vascular bundles | Plant internodes. | Male fl. state. | | Fem. fl. state. | | Red fr. state. | | |
|---|---|---|---|---|---|---|---|---|
| | 1. | 8 | 8 | 10 | 8 | 10 | 6–7 | 8 |
| | 2. | 9 | 8 | 10 | 10 | 10 | 10 | 10 |
| | 3. | 10 | 8 | 10 | 10 | 10 | 10 | 8 |
| | 4. | 10 | 10 | 10 | 10 | 10 | 10 | 8 |
| | 5. | 10 | 10 | 10 | 9 | 11 | 10 | 9 |
| | 6. | 9 | 10 | | 10 | 11 | 10 | 10 |
| | 7. | 10 | | | | 12 ? | 10 | 8 |
| | 8. | 10 | | | | 10–12 ? | 10 | |
| | 9. | | | | | | 10 | |

| Plant internodes. | | Male fl. state. | | Fem fl. state. | | Red fr. state. | | |
|---|---|---|---|---|---|---|---|---|
| No. of ridges | | 19 | 22 | 18 | 26 | 19 | 22 | 23 |
| Stomata | | (30) 35 to 45 (60) completely lignified | | | | | | |
| Lignified bast | Hypodermal | – | – | – | – | – | – | – |
| | Mesocortical | –(0) | –(0) | –(0) | –(0) | –(0) | –(0) | –(0) |
| | Pericyclic [1] | – | – | – | – | – | – | – |
| | Perimedullary | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pith lignified | | – | – | – | – | – | – | – |
| Diameters (mm.) | | 2.2 × 1.2 | 1.9 × 1.1 | 1.6 × 1.0 | 1.8 × 1.1 | 1.9 × 1.1 | 1.7 × 1.3 | 1.4 × 1.1 |

[1] In mature fruiting state, the pericyclic basts occasionally become partially lignified in the last internode at base.

TABLE III.—MICROSCOPIC STUDIES OF *Ephedra distachya*, L.

| Plant* internodes. | | L. 1699. | L. 1699. | L. 1699. | | L. 1700. | L. 1700. | L. 917** | L. 2116***. |
|---|---|---|---|---|---|---|---|---|---|
| Number of vascular bundles | 1. | 8 | 8 | 8 | 8 | 8 | 8 | (1) | 8 |
| | 2. | 8 | 8 | 8 | 8 | 9 | 8 | (10) | 8 |
| | 3. | 8 | 8 | 9 | 10 | 8 (?) | 8 | (10) | 8 |
| | 4. | 10 | 9 | 9 | 10 | 10 | 9 | (10) | 8 |
| | 5. | 10 | 10 | 10 | | 9 | 10 | (10) | 8 |
| | 6. | 10 | 10 | 10 | | 10 | 10 | | 8 |
| | 7. | 10 | 10 | 10 | | | 10 | | 9 |
| | 8. | 10 | 10 | 9 | | | 10 | | 9 |
| | 9. | 10 | 10 | 10 | | | 10 | | 10 |
| | 10. | 8 | | 8 | | | | | 10 |
| | 11. | | | | | | | | 10 |
| | 12. | | | | | | | | 10 |
| | 13. | | | | | | | | 10 |
| No. of ridges | | 19–21(25) | 24–26 | 22(24–26) | | 21(25) | 23 | 23(26–28) | 32 |
| Stomata | | 31 to 41 (51); fairly well lignified | | | | | | | |
| Lignified bast | Hypodermal | – | – | – | | – | – | – | – |
| | Mesocortical | –(0) | –(0) | –(0) | | –(0) | –(0) | –(0) | –(0) |
| | Pericyclic | – | + in 9th internode | – | | – | – | – | – |
| | Perimedullary | + | + | + | | + | + | + | + |
| Pith lignified | | + | + | + | | + | + | + | + |
| Diameters (mm.) | | 2.2 × 2.0 | 1.6 × 1.5 | 1.8 × 1.8 | | 1.9 × 1.7 | 1.5 × 1.4 | 2.0 × 2.0 | 2.2 × 2.1 |

* All plant samples are without flowers or fruit and fairly or very mature.
** L. 917, branch broken, and the first few internodes appear to have fallen off.
*** L. 2116, not definitely identified; but in all probability *E. distachya*.

TABLE IV.—MICROSCOPIC STUDIES OF *Ephedra equisetina*, BGE.

| Plant internodes. | | Male fl. state. | | Fem. fl. state. | | | Red fr. state. | | Sept. plant. |
|---|---|---|---|---|---|---|---|---|---|
| Number of vascular bundles | 1. | 7 | 8 | 6 | 10 | 7 | 8 | 7 | 6 |
| | 2. | 8 | 8 | 7 | 10 | 8 | 8 | 9 | 6 |
| | 3. | 8(9) | 8 | 8 | 10 | 8 | 10 | 10 | 6 |
| | 4. | 10 | 8 | 8 | 10 | 8 | 10 | 10 | 9 |
| | 5. | 8 | 8 | 9 | 9 | 8 | 10 | 10 | 10 |
| | 6. | 9 | 10–11 | 10 | 9 | 8 | 8 | 8 | 10 |
| | 7. | | | 10 | | 8 | | | 10 |
| | 8. | | | 10 | | | | | 10 |
| | 9. | | | | | | | | 10 |
| | 10. | | | | | | | | 10 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| No. of ridges | | 30 | 24 | 25 | 31 | 24 | 24 | 34 | 23 |
| Stomata | | DO NOT STAIN CLEARLY | | | | | | | |
| Lignified bast | Hypodermal | − | − | − | − | − | − | − | − |
| | Mesocortical | + | + | + | + | + | + | + | + |
| | Pericyclic | + | + | + | + | + | + | + | + |
| | Perimedullary | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pith lignified | | + | + | + | + | + | + | + | + |
| Diameters (mm.) | | 1.5 × 1.6 | 1.5 | 1.5 × 1.4 | 1.4 | 1.2 | 1.4 | 1.3 | 1.6 × 1.4 |

### III. CHEMICAL ANALYSIS.

While we are making a separate report of our chemical analyses it is considered of value here to give the results for total ash and acid insoluble ash which show such a big difference for the two commoner commercial species *E. sinica* and *E. distachya*. The roughness of the surface of the stems led us to suppose that certain mineral constituents would be present in larger amount in these two species which show under a low power lens sand-like particles upon the stem. Mr. Mei Ping-fu has kindly performed the analyses reported in Table V; the results are the average of at least three determinations of each species. It is clear that the earlier analyses reported in THIS JOURNAL, 14 (1925), 189, from these laboratories were done upon *E. sinica* for the insoluble fraction amounted to 18.78 per cent of the ash. At that time Mahuang was identified by the obsolete term *Ephedra vulgaris*, and we had no detailed information to hand concerning the various botanical species upon the Chinese market. For the sake of convenience we give in Table V the essential differences between the three species.

TABLE V.—ESSENTIAL DIFFERENCES OF THREE CHINESE EPHEDRA.

*A. Macroscopic.*

| Plant observations. | *E. sinica.* | *E. distachya.* | *E. equisetina.* |
|---|---|---|---|
| Length of internode | 3–6 cm. | (2) 2.5–6 cm. | 1–2.5 cm. |
| Leaf | 4 mm. long; tip recurved | 4 mm. long; often fissioned to base | 2 mm. long; close to node, dark lamina |
| Shape of stem | Flattish | Roundish round | Round |
| Surface of stem | Roughish | Rough | Very smooth |

*B. Microscopic.*

| General outline. | Angulate. | Angulate. | Undulate. |
|---|---|---|---|
| Number of ridges | (19), 22–23, (26–30) | (19), 22–23, (26–28) | 23–25, 31–34 |
| Number of bundles | 6–10 | 8 (constant) (never seen below) | 6–8 (10) |
| (2nd internode) | (Not constant) | 8 in any internode | (Not constant) |
| Stomata | (30) 35–45 (60) clearly stained | 31–41 (51) fairly clearly stained | Usually not clearly stained |
| Lignified bast: Hypodermal | − | − | − |
| Lignified bast: Mesocortical | −(0) | −(0) | ++ |
| Lignified bast: Pericyclic | − | − | ++ |
| Lignified bast: Perimedullary | 0 | ++ | 0 |
| Pith lignified | − | ++ | ++ |
| Diameters | 1.07–1.13 × 1.5–2.1 | 1.6–2.1 | 1.27–1.55 |
| Differences between the 2 diameters | 0.6–0.8 mm. | 0.1–0.2 mm. | 0–0.1 mm. |

*C. Analytic.*

| Ephedra. | | | |
|---|---|---|---|
| Total ash in dried material | 9.77 | 8.20 | 6.55 |
| Acid insoluble ash in dried material | 2.23 | 0.42 | 0.28 |

REMARKS.

1. It is interesting to note from the histological tables that whether the surface of the stem is rough or smooth does not depend upon the number, but the acuteness of the ridges, each of which is supported within by a hypodermal stereom. Thus, if there is any difference at all between the number of ridges to the stem, that of *E. equisetina*, although it is the smoothest of the three, is on an average higher than in the other two species.

2. The number of stomata is of little significance for identification purposes, although the partial or complete response to the phloroglucin stain is suggestive.

3. The differences in lignification are not to be considered a matter of chance. Any one familiar with the habit and the habitat of the three species of Ephedra can easily see why the tissues of *E. equisetina* are more lignified than the other two species. It is not only a taller plant, bearing cauline branches on a woody stem, but it is also generally found on rocky beds on high cliffs. Therefore it needs strength for its support.

CONCLUSIONS.

1. *Ephedra sinica* is distinguished by (1) its herbaceous character; (2) its ancipital branches (shown by the big difference between the long and the short diameters); (3) its whitish and recurved leaf-scales; (4) its cellulose pith and basts; (5) the presence or absence of cellulose mesocortical basts; (6) the absence of perimedullary basts; and (7) the high percentage of acid insoluble ash.

2. *Ephedra distachya* is distinguished by (1) its roundish and rough branches; (2) its lignified pith; (3) its cellulose basts, except the perimedullary, which when present are lignified; (4) the presence or absence of cellulose mesocortical basts; (5) high ash value but small insoluble fraction.

3. *Ephedra equisetina* is distinguished by (1) its woody main stems; (2) its very smooth and round branches; (3) its short internodes, less than 2 cm. long; (4) its very short and close leaf-scales; (5) its lignified pith and all the basts except the hypodermal; (6) the presence of numerous mesocortical basts; (7) the absence of perimedullary basts; and (8) low ash values.

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# PHYTOPHARMACOLOGICAL EXAMINATION OF EPINEPHRINE AND EPHEDRINE.

BY DAVID I. MACHT.

## INTRODUCTION.

The alkaloid ephedrine bears so many points of resemblance to the alkaloid epinephrine, especially in regard to its vaso-constricting properties, that it has been styled by some practising physicians and by the laity as "vegetable adrenalin." This resemblance between the two drugs is not altogether a superficial one because the pharmacological action of the two is also, in many respects, similar, so that the earlier workers with ephedrine believed that its pharmacodynamics was identical with that of epinephrine. Thus Chen (1) and Kreitmair (2) assumed that ephedrine, like epinephrine, stimulated the myoneural junctions (commonly spoken of as nerve endings) of the true sympathetic nervous system, and in that way produced its characteristic pharmacological effects. On the other hand, other investigators have found certain points of difference in the actions of the two alkaloids and have questioned, for that reason, the exact mechanism of ephedrine action as being identical with that of epinephrine. Thus, for instance, Nagel (3) has failed to obtain any inhibition of the intestinal movements after ephedrine, which some of the earlier writers claimed produced a relaxation of the same. The sympatico-mimetic action of ephedrine has also been called in question by De Eds and Butt (4), Gradinesco (5), and very recently, by Halsey (6). The present writer has also called attention to the interesting difference between ephedrine and epinephrine in their action on the bladder, which is described elsewhere (7). In the present paper the author wishes to call attention to the very interesting striking difference in pharmacological action between ephedrine and epinephrine on plant protoplasm.

## PHYTOPHARMACOLOGICAL.

The author and his collaborators have been engaged for many years in a comparative study of the reactions to drugs on animal and plant protoplasm. It was found, as set forth in various publications, that certain drugs were more poisonous for living animal preparations than for living plant tissues and, vice versa, other drugs were more toxic for living plant protoplasm than for living animal protoplasm. It was further demonstrated that in many cases living animal test objects were more sensitive to poisons derived from the plant world than to poisons of animal origin, on the one hand, and on the other hand, living plant preparations were extremely sensitive to certain poisons produced by animals and were not at all so sensitive to small doses of drugs or poisons derived from the vegetable kingdom. Thus it was found that whereas cocaine was very toxic for living animal tissues, it was comparatively little toxic for living plants (8). Such differences in reaction between animal and plant preparations have led to the discovery of certain animal toxins which were hitherto undemonstrable. Thus Macht and his co-workers have shown the presence of a toxin in the blood of menstruating women (9). Again by phytopharmacological methods, the presence of a toxin in the blood of pernicious anemia could be absolutely demonstrated and methods for differentiation between pernicious anemia and other anemia states have thus been developed which are of clinical importance (10), (11), (12).

In the present investigation, the author examined the action of epinephrine and ephedrine on living plants. The methods employed were exactly the same as those employed in other studies published by Macht and his co-workers elsewhere (13). Living seedlings of *Lupinus albus* were grown in nutrient plant physiological solutions and the increment of the single, straight, well-demarcated roots was measured. In this way the rate of growth of the Lupinus roots for a series of seedlings was studied in normal physiological solution, on the one hand, and the growth of another similar series of Lupinus seedlings from the same batch of plants was studied at the same time in physiological saline solution to which different quantities of the drugs to be examined were added. It was found that the action of small quantities of epinephrine and ephedrine hydrochlorides did not change the hydrogen-ion concentration of the solutions, as compared with the normal physiological solution, to any appreciable extent, and certainly not at all sufficiently to produce a change in the rate of growth.

On comparing the effects of ephedrine and epinephrine on the growth of the seedlings, marked differences between the two were noted. It was found that ephedrine was very little toxic for the Lupinus seedlings, whereas epinephrine was very toxic for such seedlings. Some of the results thus obtained are exhibited in the subjoined table.

TABLE I.—TOXICITY FOR GROWTH OF LUPINUS ALBUS.

| Preparation. | Concentration. | Phytotoxic index. | Preparation. | Concentration. | Phytotoxic index. |
|---|---|---|---|---|---|
| Epinephrine A | 1: 5,000 | 7% | Ephedrine A | 1: 1,500 | 75% |
| Epinephrine A | 1:10,000 | 16% | Ephedrine A | 1: 3,000 | 80% |
| Epinephrine B | 1:10,000 | 14% | Ephedrine A | 1: 5,000 | 84% |
| Epinephrine C | 1:10,000 | 13% | Ephedrine A | 1:10,000 | 88% |
| Epinephrine A | 1:15,000 | 19% | Ephedrine A | 1:10,000 | 86% |
| Epinephrine A | 1:20,000 | 35% | | | |
| Epinephrine A | 1:30,000 | 38% | | | |
| Epinephrine A | 1:40,000 | 73% | | | |

It will be seen, on examining the data, that a solution of epinephrine, 1:5000 almost completely inhibited the growth of the plants. Concentrations of 1:10,000 and 1:15,000 were also very markedly toxic, and even solutions of 1:40,000 produced a distinct inhibition as indicated by the phytotoxic index. On the other hand, solutions of ephedrine, 1:10,000, produced much less inhibition than epinephrine, 1:40,000, and even concentrations of ephedrine, 1:1500, gave a better growth than epinephrine, 1:40,000.

The writer has examined different specimens of epinephrine solutions and also prepared a solution of epinephrine of the highest purity, obtained from Professor John J. Abel, and the toxicity for *Lupinus albus* was noted with all of them. Some of the solutions examined contained chloretone as a preservative and in examining such preparations, proper controls were made with Shive solution, containing the same percentage of chloretone as the epinephrine solutions used. In addition to the experiments performed with the ordinary levo-rotatory epinephrine, the writer made a few experiments with a solution of racemic or *DL*-epinephrine, a small quantity of which he had in his possession. It was found that the racemic form was less active than the levo-rotatory form of epinephrine. An examination of the various commercial solutions of epinephrine, revealed the interesting fact that out of four

different makes which were examined, three were of very nearly the same potency. A fourth specimen, however, showed much less toxicity for the plants.

## DISCUSSION.

A comparative study of solutions of epinephrine and ephedrine hydrochlorides on the growth of *Lupinus albus* by the author's phytopharmacological methods, reveals a very interesting fact. The epinephrine was found to be very much more toxic than ephedrine which, in many respects, has a very similar action to that of epinephrine when tested by ordinary zoöpharmacological methods. These findings are of special interest when examined in connection with data obtained by the present author in regard to the action on plants of certain other drugs of animal origin, on the one hand, and of plant origin, on the other. Thus, for instance, the author has found that the powerful heart drug or poison, bufagin, isolated by Abel and Macht from the secretions of the tropical toad, *Bufo Agua* (14), is chemically and pharmacologically very similar to digitoxin, the active principle of digitalis. When, however, a solution of bufagin was compared with a solution of digitoxin on living plant tissues, it was found that the former was much more toxic (15). Again, the author has recently shown in a comparative study of cantharidin and ricin on plant protoplasm that cantharidin is extremely toxic for plants, whereas ricin, one of the most powerful poisons for animals known, is practically non-toxic for the same plants (16). In the present work, we find again that epinephrine, the drug of animal origin, is much more toxic for plants than the similar drug, ephedrine, which is derived from plants.

## SUMMARY.

1. A comparative study of epinephrine and ephedrine by phytopharmacological methods shows that epinephrine is much more toxic for plants than ephedrine.

2. Examination of various samples of epinephrine by the phytopharmacological method affords, in experienced hands, a method of not only distinguishing this alkaloid from ephedrine but also of evaluating the activity of different samples of epinephrine.

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# STUDIES IN BIOASSAYS: "THE STROPHANTHINS AND OUABAIN."*[1]

BY CHARLES W. EDMUNDS, M.D.,[2] HAROLD W. LOVELL, A.B.[3] AND SPENCER BRADEN.[3]

In the U. S. Pharmacopœia X Strophanthin is described as a glucoside or a mixture of glucosides obtained from *Strophanthus Kombe*. Descriptions follow as to its physical properties and tests are given for its identity and purity but no statement is made as to its physiological activity. This omission is of interest inasmuch as the next article described in the book is *Strophanthus Kombe* itself and for it a biological standard is prescribed, as indeed there is for all the other members of the digitalis group of drugs. The fact that strophanthin is an amorphous glucoside, and may even be a mixture of glucosides, adds to the difficulty of establishing exact chemical standards for its purity and uniformity and would seem to make a biological assay for the substance even more desirable. Of course, if it can be shown that, even with these difficulties, strophanthin as it appears on the market, prepared for medicinal use, is of uniform strength, then no biological standard of strength is necessary. It was the primary object of this research to answer this question.

Many secondary questions were also studied in addition to the primary one concerning the uniform activity of the strophanthins. Among these subsidiary questions may be mentioned a study of the relative activity of Ouabain (Crystalline Gratus-Strophanthin) and Kombe Strophanthin and indeed of the uniformity of different specimens of Ouabain itself. The activity of the powdered digitalis recommended as an international standard by the Second International Conference on Biological Standardization was also investigated and its strength relative to the U. S. P. Standard Ouabain was determined. The activity of powdered digitalis obtained upon the open market was also studied as well as the strength of different tinctures of strophanthus. A report upon the other phases of the work than strophanthin and ouabain will appear in a later communication. Finally, it may be said that the activity of these different glucosides, powders and tinctures was studied by various and sundry methods of assay which are used more or less extensively for the bioassay of the members of the digitalis group of drugs and by this comparative study not only was the activity of the drugs themselves investigated but also additional light was thrown upon the value of the methods employed.

The specimens of ouabain and strophanthin examined were as follows:

*1. Standard Ouabain U. S. P. X* obtained from Washington. It is stable at 130° C. and begins to soften at 180° C. The ordinary ouabain of commerce, crystallized from water, contains on an average about 20% of water of crystallization while the official standard preparation is crystallized from a mixture of alcohol and ether and contains 12.5% water. This fact is important in the present study, as it explains the slight variation in activity between this preparation and specimens of ouabain obtained from other sources.

*2. Ouabain, Merck No. 10182.* This specimen was furnished by Merck & Company in 1912 and the work done upon it at that time resulted in its adoption in U. S. P. IX as the standard for the digitalis series.

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3. *Ouabain, Merck No. 186450.* Obtained about ten years ago.
4. *Ouabain, Merck No. 21974.* Purchased in 1924.
5. *Strophanthin, Crystalline Kombe, Brauns-Closson* (1). Obtained in 1912.
6. *Strophanthin, Merck No. 10977.* Vial labeled "From Kombe Seeds." Obtained from a local druggist and probably an old specimen.
7. *"Strophanthin—puriss-cyst," Schuchardt.* Laboratory specimen over 20 years old.
8. *Strophanthin, Abbott Laboratories, No. 56304.* Labeled "From Kombe Seeds." 1927 specimen.
9. *Strophanthin, Merck No. 23427.* Labeled "From Kombe Seeds U. S. P. X" 1927 specimen.

The methods of assay employed in the study of the specimens enumerated above were as follows: *First,* the official one-hour frog method. *Second,* the intravenous frog method of Smith and McClosky (2). This method is practically the official method except that the drug to be tested is injected intravenously instead of being given into the lymph sac as directed in the official method. *Third,* the four-hour frog method. This method too is like the official frog method except that the period of observation is four hours instead of one hour. The suggestion that the time of observation be prolonged was made at the International Conference on Biological Standardization referred to above. *Fourth,* the frog minimal lethal dose method of Houghton. In this method the frogs are injected with the drug late in the day and the following morning the hearts are examined for systolic standstill. *Fifth,* the cat method (Hatcher-Magnus method). In this method cats of medium size were anæsthetized with urethane given by stomach and ether given as might be necessary during the operative procedures. Cannulæ having been inserted in the trachea and in a femoral vein and artificial respiration having been instituted, the warm dilute solution of the drug to be tested was injected slowly under constant pressure into the vein. The period of injection must be between 40 and 55 minutes, the end-point taken by us being final stoppage of the heart as determined by palpitation and stethoscope. *Sixth,* the final method employed was the colorimetric method of Knudson and Dresbach (3).

Before giving the results of the assays it may be well to make a few comments upon some precautions which we have found it necessary to take in order to get uniform results, not that by mentioning these anything especially new in bioassays will be revealed. In the first place, it was early realized that the mere assay of various samples of ouabain and strophanthin was by no means the whole story. Other facts of more general application might be uncovered which in turn might add to our knowledge of the question of absorption of the drugs and of the relative toxic doses to be obtained in the different methods of assay. For these and other obvious reasons great care has been taken in carrying out the work. An unusual number of frogs has been employed and in case the results in any assay were not satisfactory it was repeated—in some cases many times—until good results were obtained.

The work under the fellowship was started in the fall of 1927 by the Fellow in Pharmacology for that year (L), and in that academic year the fundamental figures were obtained. For purposes of verification this work was repeated and amplified by the second Fellow (B) in the academic year of 1927–1928. Thus, the two sets of assays served as a check upon each other. In case individual discrepancies in the results of the two years appeared, assays were repeated as often as necessary in order

to locate the difficulty. The figures given in the following table represent what is practically an average of all the results obtained and may, we believe, be accepted as giving a fairly accurate value to each preparation. Some variations in uniform results still appear in the table and we believe that even these would be smoothed out by further assays. The whole study has served to strengthen our confidence in the value of bioassay methods, but it has at the same time emphasized the absolute necessity of exercising the greatest care in attention to the details of the assay. In the first place, healthy frogs are absolutely essential. Those we obtained in 1928–1929 were clearly superior to those used in the previous year. A matter of prime importance is the maintenance of the proper temperature of the frogs during the course of the assay as well as in the twenty-four hours previous. Judging by previous assays reported, we imagine there is more looseness in this one detail than in any other. Coöperative assay reports too often give temperature readings with very wide limits of variation. Results obtained with frogs at 17° are very different from those obtained when the animals are at 21° or 22°.

In weighing frogs good results are doubtless usually obtained, but it is conducive to greater accuracy if the frogs are lightly wiped off and the urine expressed before they are weighed. Such precautions may easily change the weight by one gram and in frogs given doses near the border line an error of one Gm. may very well be responsible for a discordant result. It is unnecessary to call attention to common sources of error such as care in the dose measurement, etc., as these will naturally be avoided by any careful worker. It is in other directions that error is likely to creep in and cause serious discrepancies. For example, in the 4- and 12-hour methods it is absolutely necessary to expose the heart in order to come to a decision as to whether it is "plus" or "negative." Especially is this true in border line cases and neglect of this precaution is disastrous. Frogs may be limp and apparently dead and yet the heart be beating slowly. Unless the heart had been exposed it would have been considered "positive."

With these introductory remarks upon assay methods, the results obtained in the assay of the specimens enumerated are given in the following table:

TABLE I.

| Specimen. | | Frog methods. Official. Mg. per Gm. | Intravenous. Mg. per Gm. | 4-Hour frog. Mg. per Gm. | M. L. D. Mg. per Gm. | Cat. Mg. per Kg. | Colorimetric. |
|---|---|---|---|---|---|---|---|
| 1. Ouabain | U. S. | 0.00045 | 0.00035 | 0.00035 | 0.00025 | 0.103 | 1 |
| 2. Ouabain | M. 10182 | 0.00045 | 0.00035 | 0.00035 | 0.00025 | 0.109 | 1.07 |
| 3. Ouabain | M. 186450 | 0.00050 | 0.00035 | 0.00035 | 0.00030 | 0.113 | 1.15 |
| 4. Ouabain | M. 21974 | 0.00050 | ..... | 0.00035 | 0.00035 | 0.105 | .. |
| 5. Strophanthin | B-C | 0.00050 | 0.00035 | 0.00040 | ..... | 0.111 | 1.15 |
| 6. Strophanthin | M. 10977 | 0.00045 | 0.00035 | 0.00035 | 0.00035 | 0.106 | 1.38 |
| 7. Strophanthin | Schuchardt | 0.00100 | 0.00065 | 0.00060 | 0.00065 | 0.247 | 1.50 |
| 8. Strophanthin | Abbott | 0.00100 | 0.00065 | 0.00070 | 0.00070 | 0.289 | 2.15 |
| 9. Strophanthin | M. 23427 | 0.00100 | 0.00065 | 0.00060 | 0.00065 | 0.255 | 2.16 |

Table I shows many interesting points which will have to be discussed separately. Considering first the results obtained by the official method, it will be seen (allowing for slight differences in results) that the glucosides fall into two groups in so far as strength is concerned—one group having a toxicity just twice that of the other. In other words, the "ouabain" group has a fatal dose of about 0.0005 mg. per

Gm. of frog weight, while in the "strophanthin" group the corresponding dose is 0.0010 mg. per Gm. There is no need to discuss individual differences from the average strengths of the ouabains mentioned except in the case of Specimens 1 and 2, which in some assays show a slightly higher toxicity than the others. This may be explained in the case of No. 1 by the low per cent of water of crystallization, as was mentioned earlier. This explanation, of course, will not hold good for No. 2. Taken altogether, however, the figures obtained on the nine specimens show a very satisfactory degree of uniformity and a relative toxicity of the two groups of 50 to 100. Two notable exceptions to the general rule are furnished by Specimens 5 and 6 which nominally are strophanthins, but which display an activity equal to the ouabains. These will be discussed more in detail a little later.

In the *intravenous frog* method it will be seen that here, too, there are the same two groups in so far as toxicity is concerned and also that the ratio of toxicity of the one group to the other is, as before, about 100:50. In the "ouabain" group (including there also strophanthins 5 and 6 as they display ouabain activity), the results of the individual assays agree very well as do those of the "strophanthin" group. In both groups the toxic dose required by the intravenous route is about 35% less than that required by the lymph sac route.

By the *four-hour frog* method the results obtained upon the ouabain group were remarkably uniform and the doses approach very closely those found by the intravenous method—in most instances being exactly the same. This is perhaps what would be expected, as ample time is available for absorption and all the glucoside is taken into the circulation just as when the drug is given intravenously. Within the strophanthin group the variation in dosage is slightly greater by this method than in the intravenous or in the official method. It may be said that in the case of these relatively weak strophanthins we have had more difficulty in establishing a fatal dose than in any other instance. Especially is this true when the longer periods of observation are concerned.

The M. L. D. method yielded rather irregular results which may be partly explained by the fact that they were obtained by only one of the workers (B), and thus there was no check by the second Fellow as in the case of the other assays. Discrepancies were therefore not eliminated by getting an average of two sets of figures as in the other instances. However, they show again the 100 to 50 ratio in activity between the two groups.

The four frog methods taken together, therefore, are absolutely conclusive in demonstrating the 100 to 50 ratio in activity existing between the two groups of glucosides designated for convenience the "ouabain" group and the "strophanthin" group.

When the results obtained by the *cat* method are studied, the same general relationship in activity which is shown by the frog methods is also found here. The actual figures obtained by us are in many cases slightly higher than those published by some other workers, but this is probably due to the fact that in every case we waited for the final standstill of the heart—proving it by palpitation and by the stethoscope. Some workers using this method and taking blood pressures at the same time have made their final reading when the pressure first fell to zero. This is, however, often not the final picture as usually with members of this series the heart will stop for a brief period and then start again and maintain a fairly satis-

factory circulation for a short time. By taking the reading when the heart finally stops the figures will naturally run a little higher when this method is used. Even so, the relationship is close as Hatcher's (4) figure for ouabain of 0.1 mg. per Kg. of cat weight is quite close to our average of four specimens of ouabain of 0.108 mg. per Kg. Here, too, strophanthins 5 and 6 fall into the ouabain group, leaving no doubt whatsoever as to where they belong in so far as toxicity is concerned. The remaining three strophanthins (7, 8 and 9) again display their relative weakness, which indeed appears to be much greater by this method than by the frog methods. Specimens 7 and 9 agree with each other, but in No. 8 there is a considerable discrepancy. It is true that only five cats were used in the assay of this specimen and it is quite possible that the use of a larger number might have brought the results into closer agreement with Nos. 7 and 9. The period of time during which the injection is made in this method is very important in determining the fatal dose, but in this case (No. 8) the three cats which died in approximately the same time gave rather widely divergent figures and the average of these three gave a fatal dose of 0.302 mg. It is irregular results such as these which are so discouraging in the use of the cat method. The results obtained by this method in the first six specimens are good but the last three do not stand in proper relation to the earlier groups as judged by all the frog assays, and then again No. 8 is a marked exception in its own group.

The *colorimetric* results are still more discouraging. The results on 1, 2, 3 and 5 are quite good; No. 6 shows marked deviation from its group and approaches No. 7, when by all the biological methods it is at least twice as strong as 7. Nos. 8 and 9 show good agreement but while No. 7 should agree with them, as a matter of fact there is a very great discrepancy. Figures such as these would not give any encouragement to the adoption of this method of assay. It should be said that all these observations were made by one person and in every instance readings were made up on duplicate specimens.

Considering now strophanthins Nos. 5 and 6, it was found that they had an activity corresponding exactly to the members of the ouabain group. No. 6 is labeled as being Strophanthin "made from Strophanthus Kombe," and yet it is twice as active by every test as is the specimen of strophanthin No. 9 made also from Strophanthus Kombe by the same firm. A similar interesting situation has evidently been encountered in other quarters, as a manufacturer of large quantities of strophanthin stated in a personal communication that his firm make their product from identified Kombe seeds and that by the official method it usually had a M. S. D. of 0.0010 mg. per Gm. of frog weight, equivalent to 0.0005 mg. of ouabain. (Our assays of the product confirm these figures.) But he said that "several times the finished product made from Kombe seeds according to the same process of manufacture has been double strength; that is, the M. S. D. has been the same as that of ouabain." He stated also that they have never had a product with the M. S. D. between these two figures. This peculiar fact is confirmed in our work by the figures given in Table I. The manufacturers further state that they have no explanation to offer unless it be that Kombe seeds as purchased upon the market vary in glucosidal content. However, it is not likely that the variation would be always in the ratio of 50 to 100 and never any ratio between these two figures. It would seem that the explanation would have to be sought elsewhere, and probably in the failure to identify properly the seeds.

Specimen No. 5, "Crystalline Kombe-Strophanthin," offers special difficulties. This strophanthin specimen is part of the original lot isolated by Brauns and Closson (1) in work reported in 1913. The same product has been studied recently from the chemical standpoint by Jacobs and Hoffmann (5). They found that it was in reality a mixture which could be separated into a chloroform-soluble and a water-soluble portion. They were able to show also that the chloroform-soluble portion was identical with cymarin of Canadian hemp. From the water-soluble portion they obtained K-Strophanthin-*B* and an amorphous glucoside or mixture of glucosides. Jacobs and Hoffmann say that it is obvious that extracts of Kombe seeds contain a mixture of strophanthidin glucosides and that it is not at all certain that previous workers have worked with a homogenous substance, even when working with identified seeds.

We have touched briefly upon the chemistry of this glucoside and the opinion of the workers mentioned above regarding the possible lack of uniformity of extracts made from Kombe seeds, as it may furnish a clue to the solution of some of the discrepancies we have encountered and discussed above. It does not, however, offer an explanation of our findings on Specimen No. 6. This, according to our figures, in so far as its toxicity is concerned, belongs in the "ouabain" group. By the frog methods, by the cat method and finally even by the colorimetric test it is of "ouabain" strength. This is surprising in view of the assay of the same glucoside by Brauns and Closson. For example, Table I in their paper gives for Merck's ouabain a M. L. D. for frogs (as determined by the Houghton method) of 0.00042 mg. and 0.0010 mg. for the Crystalline Kombe Strophanthin; a ratio of 4 to 10. By the official one-hour frog method, the M. S. D. was found to be 0.0013 mg. The results obtained in the various assays led them to conclude that their crystalline Kombe Strophanthin has about half the activity of crystalline Gratus Strophanthin (ouabain). There seems to be no explanation for this interesting discrepancy between the Brauns and Closson's results and our own. On the one hand, assays made sixteen years ago by them employing two methods show a toxicity ratio between ouabain and crystalline Kombe Strophanthin of about 2 to 1. Assays made to-day upon the same specimen by six different methods, all agreeing among themselves, show a toxicity ratio of 1 to 1. That these latter figures are correct is made still more certain by the fact that our results were reported to one of the most experienced workers in this country, and at our request he assayed the specimen and found that with a M. S. D. for U. S. P. ouabain of 0.00055 mg. the dose for Brauns and Closson strophanthin was 0.00060 mg. He thus confirmed our findings. As a matter of fact, it has been found impossible to duplicate the Brauns-Closson's figures.

Since the above work was completed we have, through the kindness of Dr. Jacobs, obtained a specimen of his crystalline K-Strophanthin, the equivalent of the Brauns-Closson's product. The specimen was very pure as it had been carefully purified by repeated recrystallization at the time when it was not suspected that it was a mixture. Biological assay of this product by the one-hour and by the four-hour frog method gave a toxicity per Gm. of frog as follows:

| | |
|---|---|
| One-hour frog method | 0.0005 mg. |
| Four-hour frog method | 0.00045 mg. |

These figures, as will be seen, agree almost exactly with those we obtained using the original Brauns-Closson's specimen.

By the M. L. D. method, Brauns and Closson found an average toxicity for their product of 0.00096 mg. per Gm. of frog as compared with our figure of 0.00045 mg. per Gm. for the Jacob's product, thus emphasizing again the discrepancy between our figures and those of Brauns and Closson.

### CONCLUSIONS.

Strophanthin exists on the market to-day in at least two strengths differing greatly from each other in toxicity, one being practically twice as strong as the other. It seems justifiable, therefore, and indeed absolutely necessary to insert in the description of Strophanthin in the next revision of the Pharmacopœia a statement regarding its physiological activity.

The ouabains on the market appear to be of uniform activity and practically twice as strong as strophanthin.

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## REPORT ON THE AVAILABILITY OF CERTAIN NEW BIOLOGICALS.

BY J. C. PEACOCK.*

Since the definite service of pharmacy is to provide and dispense remedial agents, it seems appropriate to report to this Section on the availability of new materia medica as the same comes into the market.

New biological products mean new medical progress, for the ability to combat and control disease has steadily gathered strength with the practical application of succeeding discoveries in this field; and pharmacists who are endeavoring to keep up with the onward march of the medical sciences are desirous of getting a better working knowledge of this class of remedies.

The mystery in which the packages of biological agents have been all too generally enveloped can be dispelled by a better comprehension of the nature of these preparations which are so intimately associated with the treatment of disease and the protection of health.

In a paper entitled "Biologicals Viewed as Pharmaceuticals" which this writer presented last year to the Section on Practical Pharmacy and Dispensing, the suggestion was made to look upon biologicals just as other pharmaceuticals are regarded; that is, to consider them with respect to their proximate composition, as preparations of the active factors or influences which they represent, in the same way that galenicals are thus thought of by the pharmacist, as he dispenses the latter.

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* Presented to the Scientific Section, A. PH. A., Portland, Maine meeting, 1928.

The medical profession is taking the lay public more and more into its confidence on health matters and means of dealing with disease; consequently when such remedies as new biological products become commercially available the fact may well be heralded by this and other pharmaceutical associations to the pharmacist who in turn can relay this news to physician patrons and lay customers.

Such program of information must always be one of the practical services to be encouraged and promoted by organized pharmacy; for the publicity essential to the success of its votaries is constantly asking for the better education of all concerned with the remedies to be used.

Since the last meeting of this ASSOCIATION the following biologicals have been developed to the stage of commercial availability:

Diphtheria Toxoid; Perfringens (Gas Gangrene) Antitoxin; Johnin; Antivenin, Bothropic—Tropical American Anti-Snake-Bite Serum; Antivenin (Veterinary)—North American Antivenin for veterinary use; Streptococcus Cardioarthritidis Antigens and Anti-Serums; Antibrucella Serum, Polyvalent (Antimelitensis Serum or Malta Fever Serum); Tetanus Antitoxin, Bovine; and Diphtheria Toxin-Antitoxin Mixture made with goat serum.

This report is intended only to inform the pharmacist on such practical considerations of the above-mentioned products as those of designation, synonymous names, indication, nature, action, strength, style and size of container, dosage, method of administration and related aspects.

The circulars of directions which accompany these products will be found of much practical help in the administration of them.

Cataloging these new biologicals in the order in which they have appeared in the market, they are as follows:

*Diphtheria Toxoid* (Anatoxine-Ramon) is a non-toxic modified diphtheria toxin used for active immunization against diphtheritic infection. It is prepared by the action of formaldehyde on diphtheria toxin which has been made in the usual way. By this treatment, the toxin loses all of its toxic or poisonous character as ordinarily determined by guinea-pig inoculation, but retains its immunizing or antigenic powers.

The toxoid is diluted with salt solution to reduce undesirable local reactions which a full strength solution would characteristically produce.

To avoid possible confusion with the term Antitoxin, Diphtheria Anatoxine, as it is called in Europe, is known as Diphtheria Toxoid in America. The products are identical.

Toxoid differs from Toxin-Antitoxin Mixture, in that the former is diphtheria toxin *Modified* by the action of formaldehyde, while the latter is diphtheria toxin *Neutralized* by Diphtheria Antitoxin. Toxoid is therefore free from serum proteins, which is its obvious advantage over Toxin-Antitoxin Mixture.

In France especially, Toxoid has found extensive use on account of this freedom from horse serum protein and because of the observation that active immunity is produced in three to eight weeks or in about one-fourth the time required for Toxin-Antitoxin Mixture; also, because fewer doses are needed.

Diphtheria Toxoid is given subcutaneously, preferably in the back between the shoulder blades in two doses of 1 cc. each, with an interval of 3 weeks.

Diphtheria Toxoid is supplied in packages of two 1-cc. ampul vials, enough for

one immunization; and in packages of twenty 1-cc. ampul vials, enough for ten immunizations. In each package of Diphtheria Toxoid there is included an ampul vial with Green Label marked "Diluted Diphtheria Toxoid for the Reaction Test," and containing Diphtheria Toxoid diluted 1 to 20 with salt solution.

It is believed that the duration of immunity is equally long for Toxoid as for Toxin-Antitoxin.

*Perfringens Antitoxin* (Anti-Gas-Gangrene Serum) is an antitoxic serum prepared from the blood plasma of horses highly immunized against the toxin of *Bacillus Perfringens*, or *Bacillus Welchii*, which is recognized as the primary cause of gas gangrene.

In 1917, Bull and Pritchett prepared Perfringens Antitoxin that gave good results. Consequently this serum is sometimes asked for under the name of Bull or Bull's Serum. Continued work has improved this product until now an unconcentrated antitoxin may be had containing one antitoxic unit per cc. of serum. The U. S. Hygienic Laboratory has set that strength as a minimum standard for Perfringens Antitoxin.

One unit is the amount of antitoxin necessary to neutralize 1000 M. L. D. of Welch toxin. M. L. D. is the minimum lethal dose of toxin that will kill a 300-Gm. pigeon.

This standard antitoxin is produced in commercial quantity and is offered in the unconcentrated form in 100-cc. bottles including at least one antitoxin unit per cc.; and at times may be had in bottles of 50 cc. containing at least two antitoxic units per cc.

Perfringens Antitoxin is concentrated by the usual methods of globulinization until five times as strong as the unconcentrated. This refined product is marketed in syringes containing 20 cc. of concentrated antitoxin containing at least five antitoxic units per cc. or 100 units.

An initial dose of 40 to 100 units intramuscularly, followed at once in severe cases by another 40 to 50 units intravenously is usually employed. Thereafter, 40 to 80 units, intramuscularly, each day as indicated. The concentrated antitoxin is preferable because of its smaller volume. Surgical consideration may be necessary in some cases in which Perfringens Antitoxin is indicated. In doses of 25 or more units, this antitoxin is much used as a prophylactic with or without surgical procedure.

*Johnin* is an agent for the diagnosis of Johne's disease or chronic infectious dysentery in cattle.

The organism causative of this disease is now known as *Mycobacterium paratuberculosis*. It is an acid-fast organism entirely distinct from the tubercle bacillus, although resembling the latter in its staining properties.

A very full account of this diagnostic agent, by Dr. H. K. Wright of the Veterinary Department of the Mulford Laboratories, will be found in the April 1928 issue of the *Journal of the American Veterinary Medical Association*.

The history of the development of Johnin, together with method of preparation, statement of dosage and technique of application, as also mention of the symptoms suggesting its use, reports of field tests on known-infected herds and an interpretation of its effects and practical value, are given in full and careful detail.

While private veterinary practitioners are interested in this disease, the state

veterinarian, or state livestock sanitary official, is particularly concerned, since an attempt is being made to eradicate the disease along the same lines as bovine tuberculosis through the coöperation of the state and national governments. Only qualified veterinarians should administer Johnin. It is supplied in vials of 25 cc. (5 tests) and 100 cc. (20 tests).

*Antivenin* (Bothropic), Tropical American Anti-Snake-Bite Serum, is a purified and concentrated serum globulin obtained from the blood of horses which have been highly immunized against the venom of tropical American serpents of the genus Bothrops, especially against that of the "Fer-de-lance" (or *Barba amarilla* —Yellow Beard) (*Bothrops atrox*), the most dangerous snake of the mainland of tropical America from Mexico to Venezuela, and against the venom of the Horned Palmed Viper and Hog Nosed Viper.

A year ago the availability of Antivenin Nearctic, a polyvalent North American Anti-Snake-Bite serum was reported to this ASSOCIATION, and on November 10, 1927, Antivenin Bothropic, the corresponding specific serum against the venom of these common tropical American snakes was licensed for manufacture and sale.

A minimum standard has been established requiring that each cc. of Antivenin (Bothropic) neutralizes 1 mg. of venom of the "Fer-de-lance" (*Bothrops atrox*).

Antivenin (Bothropic), like North American Anti-Snake-Bite serum, is supplied in 10-cc. syringe packages, which is an average dose, with the same dating of five years, and in every other respect is comparable to North American Anti-Snake-Bite serum. The package is furnished with directions in both the English and Spanish languages.

Antivenin (Bothropic) is specific medication and therefore like Antivenin (Nearctic) makes non-specific treatment entirely unnecessary.

*Antivenin* (Veterinary).—North American Antivenin for the treatment of snake bite in animals. This product which is unconcentrated North American Anti-Snake-Bite serum is derived from the blood of horses artificially immunized against the venoms of the poisonous North American serpents of the zoölogical family Crotalidae, including rattle-snakes, the copperhead and the moccasin. In contradistinction to Antivenin for human use, which is concentrated, Antivenin (Veterinary) is unconcentrated.

Since the announcement of Antivenin Nearctic something over a year ago, Antivenin, Veterinary, has been made available for use on animals.

While the human antivenin is entirely suitable for use on animals, it has been practicable to furnish an unconcentrated Antivenin at a greatly reduced price, thereby putting this specific remedy as insurance against loss into the hands of stock owners and others interested in saving the lives of animals that are bitten by poisonous snakes in Canada, the United States and North-Central Mexico.

This service will apply to valuable hunting and other dogs as well as to live stock in general.

Antivenin (Veterinary) is prepared in the same manner and with the same exacting care as Antivenin for human use. Antivenin (Veterinary) is supplied unconcentrated in vials of 50 cc., representing the quantity necessary for an average dose. Although unconcentrated, this serum is accurately standardized and is rich

in the specific protective substances. Veterinary Antivenin is injected either subcutaneously or intravenously.

This dosage may be repeated within a few hours or at once in severe cases. Antivenin should always be administered as soon as possible after the bite, and the smaller the animal bitten the larger the dose and the quicker the administration should be.

Antivenin (Veterinary) may safely be used on humans, administering 50 cc. as a full dose, if the concentrated serum for human use is not available.

Like other antivenins, Antivenin (Veterinary) is not subject to return or exchange. It carries a five-year expiration date, and, when stored in a reasonably cool place, may be used at any time up to this date with the full assurance that it has not suffered any appreciable loss in potency.

*Anti-Rheumatic Fever Products or Streptococcus Cardioarthritidis Products.*—These are usually designated by the abbreviated term "S. C. A." for the identification of the Anti-sera and the soluble antigen prepared from the streptococcus cardioarthritidis.

These biologicals have resulted from the study of this organism by Dr. J. C. Small, he having constantly found this organism in the throat of rheumatic patients and associated with chorea.

S. C. A. Products are produced under authorization of the Rheumatic Fever Committee of Philadelphia in addition to the usual Government license.

*Antistreptococcus Cardioarthritidis Serum, Concentrated* (S. C. A. Serum, Equine) as used in the treatment of chorea and acute rheumatic fever, its complications and sequelae is produced in the horse's blood in a similar manner to diphtheria antitoxin. It is supplied in packages of one 10-cc. syringe with extra needle permitting dosage of 5 to 10 cc., which is injected intramuscularly. If needed, these amounts may be given two or three times at intervals of twelve to twenty-four hours.

S. C. A. Serum (Bovine) is an unconcentrated antistreptococcus serum, cardioarthritidis, which is supplied to patients who are sensitive to equine serum. This form is packaged in 20-cc. syringe.

These serums are used in treatment of acute attacks of rheumatic fever. S. C. A. Products are specific for streptococcus cardioarthritidis only, and no definite benefit can be expected in conditions due to other organisms.

In addition to the two forms of serum, Streptococcus Cardioarthritidis Soluble Antigen (S. C. A. Soluble Antigen) is offered for the treatment of sub-acute and chronic rheumatism and as a supplement to the serum. This antigen is a bacteria-free filtrate prepared from suspensions of the micro-organisms in normal saline solution. It contains the substance responsible for the reactions and in a definite concentration, which may be diluted as required. This product is used for active immunization in dilutions of 1:100 million, 1:10 million and 1:1 million. These are known as Dilutions 0, 1 and 2, and are packaged in 5-cc. vials with rubber caps to permit the withdrawal of the necessary dosage.

To prevent relapses, S. C. A. Soluble Antigen Dilution 0 is given to build up an active immunity, and should be started while the passive immunity is still high (on the third day following the last serum injection). In cases where the

serum is not used the Soluble Antigen may be used alone. Treatment is started with Dilution 0 and followed by Dilutions 1 and 2.

The antigen is also used as a diagnostic agent for the identification of patients suffering from chronic rheumatism, by subcutaneous injection.

*Antimelitensis Serum* (Antibrucella Serum Polyvalent; *Melitensis* and *Abortus*) for the treatment of Undulant or Malta Fever.

Recent investigations have established the close relationship of the causative organism of Malta Fever (*Micrococcus melitensis*) to the *Brucella Abortus* of Bang (the organism of bovine contagious abortion which has been proved to be infectious for human beings).

A serum formerly supplied under the name of Anti-Malta-Fever Serum was prepared against *Brucella melitensis* only. In the production of the present Antimelitensis-Serum or Antibrucella Serum, hyper-immunization of cattle is effected by treatment with the two types, Brucella melitensis and Brucella abortus. In immunizing cattle, the two types are kept separate, so that *antimelitensis* and *antiabortus* serums are prepared and obtained separately. These serums are then mixed in equal proportions, so that the resulting product is a polyvalent Antimelitensis-Serum which contains antibodies for both types of organisms.

Physicians may not think of the possibility of meeting Malta Fever, but typhoid or paratyphoid will be considered. Having these in mind, they will send blood for a Widal test. Experience indicates that in all such cases an examination for Malta Fever should be done.

Antimelitensis Serum Polyvalent is supplied in packages of 50-cc. double-end vials with injection outfit.

The average dose, injected intravenously, is 50 cc. to 100 cc., repeated in 12 to 24 hours, if necessary.

It is a bovine serum and can, therefore, be administered safely to individuals who have previously received the injection of serum from horses, or who may naturally be sensitive to horse serum. Individuals who are known to be sensitive to bovine serums must first be desensitized by the usual methods.

*Tetanus Antitoxin, Bovine,* is now obtainable for use on patients who have had a previous injection of horse serum, or who may be otherwise sensitive to equine protein, thus enabling the administration of Tetanus Antitoxin as an immunizing agent under these conditions.

Tetanus Antitoxin, Bovine, is considerably higher in price than that of equine origin owing to the fact that the production of the bovine product is very much smaller per animal and consequently exceeds in cost Tetanus Antitoxin that is regularly produced in larger amounts in horses.

The product so far available is concentrated or globulinized and put up in the 1500-unit syringe package, making it the counterpart of the equine antitoxin which is so commonly used in this form and strength for prophylaxis. Like the equine product, each package of Tetanus Antitoxin, Bovine, is finished with an excess of antitoxin units to allow for a two years' dating.

*Diphtheria Toxin Antitoxin Mixture* (Goat) is a mixture of $^1/_{10}$ L plus dose of toxin per cc. made with Diphtheria Antitoxin cultivated in the blood serum of the goat instead of from usual Diphtheria Antitoxin obtained from the serum of immunized horses.

In all other respects this Toxin-Antitoxin Mixture is the exact counterpart of the usual Diphtheria Toxin-Antitoxin of this strength and it is used in the same dosage, and method of administration for active immunization.

This product offers opportunity for immunization of all subjects hypersensitive to horse serum protein.

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## PHYTOCHEMICAL NOTES.*†

### No. 102. THE NON-HEPTANE CONSTITUENTS OF JEFFREY PINE.

BY P. A. FOOTE.

Early in 1927 an understanding was reached with Dr. Graham Edgar of the Ethyl Gasoline Corporation of Yonkers, N. Y. in accordance with which a large amount of Jeffrey Pine oil was to be sent to the Wisconsin Pharmaceutical Experiment Station for rectification of its principal constituent, the heptane. The non-heptane constituents were to be used for further investigation of these substances whereas the heptane fraction was to be forwarded to Yonkers for the study of the standardization of gasoline as fuel in internal combustion engines. The Jeffrey Pine oil was produced in California during the summer of 1927 as a coöperative enterprise between the Ethyl Gasoline Corporation, the local representative of the Bureau of Forestry and a third party, the California Chemical Company. The material, four drums of about 50-gallon capacity each, was received in the fall of the same year.

Through the kindness of Professor O. Kowalke, the Walter Lummus 20-gallon copper, steam-jacketed alcohol rectifying still of the Chemical Engineering Department was used. It is equipped with a 6-ft. 12-section column and dephlegmator, the latter being unnecessary for this work. The details of this fractionation have been recorded in a report submitted to Dr. Edgar, hence need not be repeated here. The densities of the numerous fractions revealed that great care had been exercised in excluding contamination with Western Yellow Pine. For the purposes of this paper it may suffice to record the summary of materials obtained, *viz.:*

I. An aqueous cohobate.
II. Oily fractions distilling below the boiling point of *n*-heptane.
III. The heptane fractions forwarded to the Ethyl Gasoline Corporation.
IV. Oily fractions distilling above the boiling point of *n*-heptane after the removal of aldehydes by shaking them with a concentrated solution of sodium acid sulphite.
V. The oily aldehydes regenerated from the sodium acid sulphite addition products.

*Isolation and Identification of the Aldehydes.*—From the numerous fractions distilling over above the boiling point of *n*-neptane the aldehydes were removed by shaking them with a concentrated solution of sodium acid sulphite. The solid addition product was separated with the aid of a force filter and the drained solid washed with petroleum ether. The aldehydes were regenerated with sodium car-

* From Scientific Section, A. PH. A., Portland meeting, 1928.
† From the laboratory of Edward Kremers.

bonate and separated by steam distillation. In this manner 1142 Gm. of material were obtained. The aqueous sulphite mother liquid (not the petroleum ether washings), when made alkaline with sodium carbonate, yielded additional 152 Gm. upon distillation. The two products were kept separate.

The 1142 Gm. of aldehydes were fractionated under a pressure of about 0.1 mm. The melting points of several thiosemicarbazones not being sharp, refractionation under the same pressure was resorted to, this time with a Vigreaux column. More than fifty fractions of one degree each were thus obtained. Yield, densities and melting points of thiosemicarbazones are recorded in the following table:

| No. | B. p., °C. | Sp. gr. at 24° C. | Wt. in Gm. | Remarks. |
|---|---|---|---|---|
| 1 | to 43 | .... | 7.6 | |
| 2 | 43–4 | 0.8193 | 92.7 | Thiosemicarbazone, m. p. 94–95° (softens at 92°) |
| 3 | 42–3 | 0.8226 | 71.2 | Slight pressure change |
| 4 | 43–4 | .... | 26.3 | |
| 5 | 44–7 | .... | 13.6 | |
| 6 | 47–8 | .... | 45.1 | |
| 7 | 48–9 | .... | 7.3 | |
| 8 | 49–50 | .... | 5.5 | |
| 9 | 50–51 | .... | 11.3 | |
| 10 | 51–2 | 0.8250 | 77.7 | Thiosemicarbazone, m. p. 90–95° |
| 11 | 52–3 | .... | 8.6 | |
| 12 | 53–4 | .... | 14.1 | |
| 13 | 54–5 | .... | 7.7 | |
| 14 | 55–6 | .... | 2.0 | |
| 15 | 56–7 | 0.8324 | 33.7 | |
| 16 | 57–8 | .... | 8.0 | |
| 17 | 58–9 | .... | 4.0 | |
| 18 | 59–60 | .... | 3.5 | |
| 19 | 60–62 | .... | 4.0 | |
| 20 | 62–3 | 0.8267 | 22.7 | Thiosemicarbazone, m. p. 75–77° (softens at 73°) |
| 21 | 63–4 | .... | 7.8 | |
| 22 | 64–5 | .... | 3.4 | |
| 23 | 65–6 | .... | 13.0 | |
| 24 | 66–7 | .... | 12.0 | |
| 25 | 67–8 | 0.8541 | 39.6 | |
| 26 | 68–9 | .... | 12.5 | |
| 27 | 69–70 | .... | 12.4 | |
| 28 | 70–1 | 0.8595 | 41.7 | Thiosemicarbazone, m. p. 97–98° |
| 29 | 71–2 | .... | 20.0 | |
| 30 | 72–3 | .... | 32.6 | |
| 31 | 73–4 | 0.8563 | 108.8 | Thiosemicarbazone, m. p. 99–100° (softens at 96°) |
| 32 | 74–5 | .... | 22.3 | |
| 33 | 75–6 | .... | 7.1 | |
| 34 | 76–7 | .... | 6.8 | |
| 35 | 77–8 | 0.8558 | 46.5 | |
| 36 | 78–80 | .... | 6.5 | |
| 37 | 80–1 | .... | 35.5 | |
| 38 | 81–2 | .... | 2.5 | |
| 39 | 82–3 | .... | 5.8 | |
| 40 | 83–4 | .... | 1.0 | |

| No. | B. p., °C. | Sp. gr. at 24° C. | Wt. in Gm. | Remarks. |
|---|---|---|---|---|
| 41 | 84–97 | .... | 6.8 | |
| 42 | 97–8 | .... | 10.7 | |
| 43 | 98–9 | .... | 8.3 | Yellow color of decomposition begins |
| 44 | 99–100 | 0.8532 | 13.5 | |
| 45 | 100–105 | .... | 6.5 | |
| 46 | 105–110 | .... | 8.2 | |
| 47 | 110–120 | .... | 3.4 | |
| 48 | 120–130 | .... | 2.8 | |
| 49 | 130–135 | .... | 4.7 | |
| 50 | 135–140 | .... | 6.1 | |
| 51 | 140–147 | .... | 21.2 | |
| 52 | 147–157 | .... | 2.8 | |
| 53 | 157–167 | .... | 7.0 | |
| 54 | 167–177 | .... | 2.2 | |
| 55 | 177–185 | .... | 2.5 | |
| 56 | Residue | .... | 11.9 | |
| | | Total | 1023.0 | |

In 1913 Schorger[1] working with the oleoresin suspected citronellal. Schimmel & Company[2] in 1914 found no citronellal but *n*-decylic aldehyde. They also suspected the lower homologues, *n*-octylic and *n*-nonylic aldehydes. The m. p. of the thiosemicarbazones prepared by them are here recorded for comparison.

FRACTION NO. 2.

| | Found. | Recorded for *n*-octylic aldehyde. |
|---|---|---|
| Boiling point. | 43–4° at 0.1 mm. (62–3° at 10 mm. estimated) | 60–63° at 10 mm. |
| Sp. gr. | 0.8193 at 24° | 0.8211 at 20° |
| M. p. thiosemicarbazone[3] | 94–5° | 94–5° |
| $n_D$ | 1.4241 at 25° | 1.41955 (temp. not given) |
| $\alpha_D$ | +0.05° at 25° | 0° |

This fraction corresponds to *n*-octylic aldehyde in the above properties, but is evidently slightly contaminated as is indicated by the slight angle of rotation. Although it absorbs a small amount of bromine, this property may be accounted for by partial enolization.

FRACTION NO. 20.

| | Found. | Recorded for *n*-nonylic aldehyde. |
|---|---|---|
| Boiling point | 62–3° at 0.1 mm. (80–82° at 13 mm. estimated) | 80–82° at 13 mm. |
| Sp. gr. | 0.8267 at 24° | 0.8277 at 15° |
| M. p. thiosemicarbazone[4] | 75–77° | 77° |
| $n_D$ | 1.4432 at 25° | 1.42452 at 16° |
| $\alpha_D$ | +0.10° at 25° C. | 0° |

[1] *Ind. Eng. Chem.*, 5, 971.

[2] *Ber.* v. Schimmel & Co. (Apr. 1915), 48.

[3] Using a 25-p. c. excess of reagent on 0.7826 Gm. of the fraction the yield was 74.5 p. c. of the theoretical assuming the aldehyde to be *n*-octylic.

[4] Using a 25-p. c. excess of reagent on 0.8379 Gm. of the fraction the yield was 61.5 p. c. of the theoretical, assuming the aldehyde to be *n*-nonylic.

This fraction would, therefore, appear to be largely *n*-nonylic aldehyde. Slight traces of impurities are indicated by the angle of rotation.

FRACTION NO. 31.

| | Found. | Recorded for *n*-decylic aldehyde. | citronellal. |
|---|---|---|---|
| Boiling point | 73–4° at 0.1 mm. (93–94° at 12 mm. estimated)[1] | 93–94° at 12 mm. 80–81° at 6.5 mm. | 89–91° at 14 mm. |
| Sp. gr. | 0.8563 at 24° | 0.8361 at 15° | 0.8554 at 17.5° |
| M. p. thiosemicarbazone[2] | 99–100° | 99–100° | 54–55° |
| $n_D$ | 1.4480 at 25° | 1.42977 at 15° | 1.4481 |
| $\alpha_D$ | +1.30 | | +8.18° to 12.30°[3] |

This fraction likewise absorbs bromine. The b. p. is close to that of both of the suspected compounds. The sp. gr. and index of refraction are close to citronellal but its optical rotation is small for the latter. Since the melting points of the thiosemicarbazones of *n*-decylic aldehyde and citronellal lie so far apart the m. p. found would indicate that only *n*-decylic aldehyde reacted with the reagent.

The data obtained for Fraction No. 31 were at first puzzling for its b. p. and the m. p. of its thiosemicarbazone were those of *n*-decylic aldehyde, yet its sp. gr. and index of refraction were very close to those of citronellal. The problem was solved several weeks later when the sp. gr. of all the fractions was found to have increased as well as their index of refraction. Polymerization had taken place. When purified by $NaHSO_3$ the regenerated aldehyde had a sp. gr. of 0.8260 at 25° C. and an index of refraction of 1.4278 at 25° C. Its thiosemicarbazone melted at 99° C. It is therefore *n*-decyclic aldehyde.

The absorption of bromine may be explained as due to the enol form of aldehyde, a well-known phenomenon.

The 152 Gm. of mixed aldehydes regenerated from the sulphite liquor upon fractionation gave:

| No. | B. p., ° C. at 0.1 mm. Hg. | Sp. gr. at 24° C. | Wt. in Gm. |
|---|---|---|---|
| 1 | 45–52 | 0.7925 | 44.3 |
| 2 | 52–6 | 0.8256 | 50.1 |
| 3 | 56–62 | 0.8536 | 12.0 |
| 4 | 62–68 | 0.8813 | 9.8 |
| 5 | 68–73 | 0.9033 | 14.3 |
| 6 | 73–100 | .... | 11.3 |
| | | Total | 141.8 |

## CONCLUSIONS.

*n*-Octylic, *n*-nonylic and *n*-decylic aldehydes have been identified.

[1] The variation appears to be 2° per mm. whence the estimations are made.

[2] Using a 25-p. c. excess of reagent on 4.2212 Gm. of the fraction the yield was 58.9 p. c. of theoretical, assuming the aldehyde to be *n*-decylic.

[3] Citronellal from Java lemon oil, —3°.

# BOOK LITERATURE ON NEW REMEDIES.*

BY LIDA WINKELBLECH AND EDWARD KREMERS.

As of the making of books, so of the making of remedies there is no end. Just as the making of books preceded the printing press by centuries if not tens of centuries, so the making of new remedies preceded the establishment of the "Farbenfabriken" by long periods of pharmaceutical history. Yet modern writers of the subject have seen the beginning of the development of new remedies so-called in the discovery of antipyrine and the numerous therapeutic syntheses that have followed. Others have gone back to the discovery of chloral hydrate by Liebig in 1832. Still others have claimed that the modern science of pharmacology is based on the discovery of the alkali-like properties of morphine by Sertürner in 1817 and the rapid isolation of other plant alkaloids which this discovery made possible. All of these writers seem to be unaware of the constant evolution that has been going on through ages and have picked out one of the numerous milestones that mark stages of a semi-revolutionary character. Even then they seem to have overlooked what is possibly the most revolutionary milestone of all, *viz.*, the one that marks the passage from the medicamentation of the school of Galen to that of the iatrochemical school of Paracelsus, a transition which was after all as slow as it was hotly contested.

These few remarks though casual will suffice, however, to reveal that a definition of what constitutes a new remedy is impracticable. The compounds of antimony, though by no means all new to the iatrochemist, were "new remedies" to the iatrophysicians. Morphine, strychnine and brucine were "new remedies" during the early decades of the past century. Iodine, hydrocyanic acid and urea became new remedies only a few years later, yet "synthetic" urea seems to have enjoyed a rejuvenation as a "new remedy" much more recently. Many other chemicals long known, but the physiological properties of which have become known since, have paraded in the literature on new remedies. Naturally, new remedies are not confined to any one of the three natural kingdoms, neither are they confined to modern synthetics. A plant that may long have been known in one country acquires new significance in another and thus enters the literature on new remedies of that country. Hence in compiling a bibliography of the literature on new remedies it will be quite impracticable to base inclusions and exclusions on any arbitrary definition. So far as the general literature is concerned the only practical solution, it would seem, is to restrict the bibliography to those treatises the titles of which suggest their inclusion.

In an era of such rapid progress as that represented by the nineteenth century, it is but natural that the designation "new" did not always satisfy the author, but that he coveted the comparative and even superlative in order to attract the attention of the prospective user of his literary ware. Yet even in this trick, whether of author or publisher, there appears to be nothing very new.

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* This preliminary report on a certain phase of the bibliography of new remedies is a supplement to a report on experimental work by Miss Winkelblech (JOUR. A. PH. A., 13 (1924), 619), made possible by a grant of the Research Committee of the AMERICAN PHARMACEUTICAL ASSOCIATION.

CHRONOLOGICAL LIST.

The following chronological list of treatises, also editions and translations thereof, is intended to reveal something of the importance of this class of pharmaceutical literature. It makes no pretense at completeness, but it is hoped that it may induce the critical reader to point out omissions and other defects. A bibliography of this subject ought not to prove unwelcome to pharmaceutical and medical librarians. Hence the coöperation of all who have any suggestions to make is sought. This chronological list will be followed by a more detailed account of the individual treatises arranged alphabetically according to the names of their authors.

1821. "Magendie." First French edition.**
1821. "Magendie." First German edition based on first French edition. (Imprint 1822.)**
1822. "Magendie." Second French edition.**
1822. "Magendie." English edition.**
1822. "Magendie." Second German edition based on second French edition.**
1822. "Magendie." Third French edition.**
1823. "Magendie." Third German edition based on third French edition. (Bears imprint of 1824).**
1823. "Magendie." (François.) Formulary for the preparation and mode of employing several new remedies.....With an introduction and notes, by C. T. Baden.....Translated from the Formulaire.....par F. Magendie....."Troisieme edition," London, 1823, 12°. (Br. Mus. Cat.)**
1824. "Magendie." Fourth French edition.**
1824. "Magendie." Fourth German edition based on fourth French edition.**
1824. "Magendie." Second (English) edition with numerous alterations and additions. By R. Dunglison. (Appendix.....by R. Dunglison), London, 1824, 12° (Br. Mus. Cat.) (Based on third French edition.)**
1825. "Magendie." Fourth (English) edition with an appendix, containing all the improvements of the fourth edition ....Paris, July 1824, etc. By R. Dunglison. 2 pt. T. & G. Underwood, 1825, 8°. (Br. Mus. Cat.)**
1825. "Magendie." First Italian edition based on fourth French edition.**
1825. "Magendie." Fifth French edition.**
*1826. Kunze, "Vorschriften etc., von Magendie." 5th German edition from 5th French edition.
1826 "Magendie." First Spanish edition based on fifth French edition.**
1828. "Magendie." Formulary of the preparation and employment of several new remedies.....Translated from the sixth eition of the "Formulaire of M. M.".....With an Appendix containing the experience of British Practitioners with many of the new remedies.....By J. Houlton. London, 1828, 12°. (Br. Mus. Cat.)**
1835. "Magendie." Formulary for the preparation and employment of several new remedies.....Translated from the eighth edition of the "Formulaire of M. Magendie," with an appendix, by C. W. Gregory, London, 1835, 8°. (Br. Mus. Cat.)**
1837. Riecke, "Die neueren Arzneimittel, etc."
1838. "Magendie's Formulary" of all the new medicines, from the last Paris edition, arranged alphabetically.....With numerous additions from the best British and foreign authorities up to the present time. London (1838) s. sh. fol. (Br. Mus. Cat.)**
*1840. Riecke, "Nachtraege zur ersten Auflage der neueren Artzneimittel."
*1840. Riecke, "Die neueren Arzneimittel." Zweite, voellig umgearbeitete Auflage."
*1842. Riecke, "Die neueren Arzneimittel." Dritte vielfach vermehrte und verbesserte Auflage. (3 Abthln. Heinsius.)

* Editions thus indicated are in the General Library of the University of Wisconsin and have been consulted in the preparation of this bibliography.

** Information concerning the numerous editions of Magendie and their translations has been obtained, in large part, from the fifth German edition of 1826 by Kunze, supplemented by data secured from the British Museum Catalogue.

*1848. Aschenbrenner, "Die neueren Arzneimittel und Arzneibereitungsformen."
1849. Aschenbrenner, "Die neueren Arzneimittel, etc." Zweite, Auflage.
*1851. Aschenbrenner, "Die neueren Arzneimittel, etc." Dritte vermehr. u. verbess. Auflage.
1861. Aschenbrenner, "Die neuesten Arzneimittel, etc." Vierte, vermehr. u. verbess. Auflage.
1879. Loebisch, "Die neueren Arzneimittel in ihrer Anwendung und Wirkung."
*1883. Loebisch, "Die neueren Arzneimittel." Zweite, gaenzlich umgearbeitete, etc., Auflage.
1888. Fischer, "Die neueren Arzneimittel."
1888. Fischer, "Die neueren Arzneimittel." Zweite vermehrte Auflage.
*1888. Loebisch, "Die neueren Arzneimittel." Dritte gaenzlich umgearbeitete, etc., Auflage.
*1889. Fischer, "Die neueren Arzneimittel." Dritte vermehrte Auflage.
*1889. Fischer, "Die neueren Arzneimittel." Vierte, vermehrte Auflage.
1891. Fischer, "Die neueren Arzneimittel." Vierte Auflage.
1891. Brestowski, "Die neueren und neusten Arzneimittel."
*1891. Heger, "Synopsis der neueren Arzneimittel."
*1891. "Helbing's Modern Materia Medica." Second[1] enlarged edition.
*1892. Brestowski, "Die neueren und neuesten Arzneimittel." Zweite, mit einem Anhang vermehrte Auflage. Bearbeitet von Brestowski.
*1892. "Helbing's Modern Materia Medica." Third enlarged edition.
*1893. Fischer, "Die neueren Arzneimittel." Fuenfte, stark vermehrte Auflage.
*1893. Schmidt, "Arzneimittel der Apotheken."
*1894. Thoms, "Die Arzneimittel der organischen Chemie."
*1894. Fischer, "Die neueren Arzneimittel." Sechste, vermehrte Auflage.
*1895. Coblentz, "The Newer Remedies."
1895. "Helbing's Modern Materia Medica." Fourth edition.
1895. Loebisch, "Die neueren Arzneimittel." Vierte, gaenzlich neu bearbeitete Auflage.
*1896. Coblentz, "The Newer Remedies." Second edition.
*1897. Mindes, "Arzneimittel Manuale."
*1897. Thoms, "Die Arzneimittel der organischen Chemie." Zweite Auflage.
*1898. Mindes, "Arzneimittel Manuale." Zweite Auflage.
*1899. Coblentz, "The Newer Remedies." Third edition.
*1899. Peters, "Die neuesten Artzneimittel und ihre Dosirung incl. Serum- und Organtherapie."
*1900. Mindes, "Artzneimittel Manuale." Dritte Auflage.
1901. Wainwright, "New Remedies and Therapeutic Measures."
*1902. Peters, "Die neuesten Arzneimittel und ihre Dosirung, etc." Dritte Auflage.
*1902. Mindes, "Manuale der neuen Arzneimittel, etc." Vierte, neu bearbeitete Auflage.
*1903. Arends, "Neue Azrneimittel und pharmazeutische Spezialitaeten, etc."
*1904. Peters, "Arzneimittel." Vierte Auflage.
*1905. Arends, "Neue Arzneimittel und Spezialitaeten." Zweite, Auflage.
*1906. Peters, "Artzneimittel." Fuenfte Auflage.
*1906. Rosenthaler, "Neue Arzneimittel organischer Natur."
*1907. Hildebrand, "Neuere Arzneimittel."
*1907. Leuders, "Die neueren Artzneimittel."
*1908. Coblentz, "The Newer Remedies." Fourth edition.
1909. Arends, "Neue Arzneimittel, etc." Dritte Auflage.
*1911. Peters, "Artzneimittel." Sechste Auflage.
*1913. Arends, "Neue Arzneimittel und Spezialitaeten." Vierte Auflage.
*1913. Bachen, "Neue Arzneimittel, ihre Zusammensetung, Wirkung und Verwendung."
1921. Bernoulli, "Uebersicht der neueren Arzneimittel und der gebraeuchlichen Spezialitaeten."

No attempt has been made to bring this list up-to-date after June 1922 when the library work on this compilation was interrupted.

P. S. Since the manuscript of this article was sent to the editor, one of us has done considerable work on the special bibliography of Magendie's Formulary, its numerous editions and translations which will result in several changes. This and other special bibliographies are to be reported as soon as completed.—E. K.

[1] The first edition did not appear in book form. See Helbing.

# PRELIMINARY STUDIES OF THE ROSENHEIM, DRUMMOND COLOR TESTS OF VITAMINE A IN COD-LIVER OIL.*

BY E. C. TOWLE AND E. C. MERRILL.

In the *Lancet* of January 31, 1928, Messrs. Rosenheim and Drummond published the results of a fairly comprehensive study of the relation between their colorimetric test for vitamine A in cod-liver oil as compared with actual biological studies made on the same samples of oil. We believe this pioneer work of Messrs. Rosenheim and Drummond constitutes a valuable line of thought which eventually will lead to the perfecting of a chemically controlled test that may be depended upon as a quick means of estimating vitamine A in cod-liver oil.

Whatever follows, therefore, should be understood as constructive suggestion devoid of criticism of the originators of the test and written with the object of bringing about a concentration of study on this test which will relegate to the background the biological test which is obviously handicapped by the factor of time alone as to be insufficient for commercial needs. In the following the authors have made a special study of the Antimony Chloride method of colorimetrically estimated vitamine A in cod-liver oil described in the *Lancet* January 21, 1928—page 148, as follows:

> Carr and Price, *Biochemical Journal*, 20 (1926), 497.
>
> "*Antimony Chloride Method.*—By means of a standard pipette 2 c.cm. of the oil are measured into a measuring flask of 10 c.cm. capacity. The pipette is rinsed out three times with chloroform, and the solution made up to volume with the same solvent; 0.2 c.cm. (= 40 c.mm. oil) of the solution are measured into a test-tube (10 mm. diameter) and mixed with 2 c.cm. of a 30 per cent antimony chloride solution in chloroform delivered from a standard burette. Readings are taken as above described. Limit of error as above."

*1.* It has been noted that in following technique of the above-mentioned test that the development of blue color and its transitional changes to an ultimate red or muddy-brown color is very positively influenced by the temperature of the reaction mixture in the test-tube. Illustrative of this reaction we may state that in conducting the test at ordinary room temperature (approximately 25° C.) the blue color develops in a few seconds time, and progressively goes through changes from a blue color developing red rapidly and fading to the ultimate red or reddish brown within a few minutes. On the other hand, if the reaction mixture in the test-tube is cooled to a temperature of 10° C. or below, the rate of change of color proceeds at a lesser rate of speed and lasts nearly 20 times longer in duration than at room temperature. With this thought in mind, it is suggested that the ultimate control of the technique of this test may be perfected by specifying a definite working temperature which will enable one to operate under sufficient margin of time to make accurate reading of the color by Lovibond Tintometer or other means.

*2.* The color reaction in the Antimony Trichloride Colorimetric test appears to consist of two stages:

*a.* The development of an intense blue color.
*b.* The fading of the blue and the development of a red color.

In this study we wish to mention the three following experiments:

* Scientific Section, A. PH. A., Portland meeting, 1928.

*Experiment No. 1.*—This test was conducted in the regular way by the Antimony Trichloride method on some cod-liver oil of known vitamin content that had been subjected to biological assay. The characteristic blue appeared at once, and faded in the usual manner in a few minutes at room temperature.

*Experiment No. 2.*—Another portion of the original biologically assayed cod-liver oil was subjected to a temperature of approximately 100° C., at the same time being treated by a continuous stream of air passing through the oil. A sample of this oil subjected to the Antimony Trichloride test showed an immediate deep red color.

*Experiment No. 3.*—A sample of the original biologically assayed cod-liver oil of definite vitamin A content was tested by the Antimony Trichloride method and a few seconds after the reaction had commenced a small quantity of zinc dust was added. The speed of this test as compared with No. 1 test, which was conducted under identical conditions of temperature, was greatly retarded in rate of development of red color.

From the above experiments we would lean to the opinion that the development of red coloration is associated with an oxidation process.

*3.* Further study of the influence of alcohol to the reaction mixture, using the Antimony Trichloride method, result in the observation that the addition of minute quantities of alcohol tend to speed up the rate of the reaction and speed of change from blue to red color. This being the case, would it not be desirable to use a chloroform that is entirely free from alcohol, since the American market medicinal or U. S. P. chloroform permits the presence of between 99 and 99½% of chloroform and the remainder consisting of alcohol.

*4.* From "Lewkowitsch's Chemical Technology and Analysis of Oils, Fats and Waxes"—page 270—we quote as follows:

> "A very delicate and characteristic reaction, described by Hager, was modified by Salkowski, as follows: A few centigrams of cholesterol are dissolved in 2 cc. of chloroform, an equal volume of concentrated sulphuric acid is added, and the mixture shaken. The chloroform solution is immediately colored blood-red, afterwards cherry-red and purple; the last tint remains for several days. (The sulphuric acid layer under the chloroform shows sometimes a strong green fluorescence.[1]) On pouring a few drops of the purple chloroform layer into a porcelain basin, the red colour changes rapidly to blue, green, and finally to yellow. On diluting the purple solution with more chloroform, it becomes nearly colourless or acquires an intense blue colour; if it now be shaken again with the sulphuric acid, the former colouration reappears. These changes of colour are said to be due to traces of water in the chloroform.[2]
>
> "If a chloroform solution of cholesterol prepared from fats be shaken with concentrated sulphuric acid, the blue colouration is noticed at once; this indicates the presence of so-called "lipochromes," which have been shown to occur in cod-liver oil, the fat of the yolk of eggs, palm oil, and in small quantities in cow butter. But even in these cases the red colouration soon appears."

We believe there is a close analogy between the test of Hager as modified by Salkowski with the Carr and Price Antimony Trichloride reaction especially in

[1] In the case of wool fat cholesterol this green fluorescence is, in the author's opinion, due to the presence of isocholesterol.

[2] According to Herbig (*Dinglers polytech. J.*, 303 (1897), 191), cholesteryl palmitate and cholesteryl cerotate give the same colour reaction.

consideration of the so-called lipochromes as described by these investigators many years prior to the recognition of the various types of vitamins. Of special interest is that portion of the above quotation describing the color test on cholesterol: "On diluting the purple solution with more chloroform, it becomes nearly colourless *or* acquires an intense blue colour." We are wondering if the record of this test on cholesterol did not actually vary with the source of the cholesterol obtained, since the writer in a foot-note states as follows:

"Wool fat cholesterol does not show the violet-pink colouration given by gallstone cholesterol, but becomes red at once."

Reverting again to the Antimony Trichloride test, we note that the behavior of this reaction is influenced in a very uncertain manner by the additions of varying traces of water from which we infer that the balance of moisture content in this reaction mixture would seem to be a desirable subject for further study.

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## A LITERATURE REVIEW ON THE PRODUCTION OF ANTIRACHITIC SUBSTANCES BY THE IRRADIATION PROCESS.*

BY ELIZABETH PICKERING.

The development of our knowledge of the antirachitic vitamin within the past five years has been remarkable. No earlier than 1922 was differentiation made between the antiophthalmic vitamin A and the antirachitic vitamin D, occurring together in butter and cod liver oil and prior to that time and even in much literature published after that time, classed together as the fat-soluble A vitamin. Now, although we do not know the exact chemical structure of the vitamin D, we know it contains only carbon, hydrogen and oxygen and a method of synthesis has been arrived at. Simultaneously, our knowledge of the etiology of its deficiency disease, rickets, has shown advance.

Prior to the discovery that certain foods could be given antirachitic potency by irradiation with ultraviolet light, those rays had been used in the therapy of rickets. This work has been reviewed by Park (172). In some cases, eosin was administered before light treatment on the assumption that its ability to absorb ultraviolet light increased its action in the body (72). Rats fed on diets deficient in fat-soluble vitamins did not develop rickets when irradiated with light from a mercury vapor quartz lamp (178) although ophthalmia due to deficiency of vitamin A was not delayed (224). More recently, the effect of sunlight (11) and of ultraviolet light (63,156) in preventing leg weakness and rickets in poultry has been studied. The biologically active wave-lengths in sunlight were found by Luce to be below 296 $\mu\mu$ (153); by Huldschinsky to be from 289 to 320 $\mu\mu$ (128); and by Hess and Weinstock using Corning glass filters to be below 303 $\mu\mu$ or possibly 313 $\mu\mu$ (198). Similar protection of rats from rickets by much more prolonged irradiation (18 times) with Wood's light (about 365 $\mu\mu$) has also been reported (166).

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* Scientific Section, A. PH. A., Portland meeting, 1928.

Almost simultaneously it was reported by Steenbock and Nelson (218, 226) and by Hess and Weinstock (89, 99) that synthetic rations (218), excreta (226), fats, (218), and oils (linseed and cottonseed (88, 89, 99) acquired ability to prevent or cure rickets in rats following ultraviolet irradiation for a period of $^1/_2$ to 5 hours (220). This property was soon traced to sterols contained in these materials. The antirachitic potency of such irradiated vegetable oils was found to reside in the unsaponifiable fraction of the oil (108, 109). Moreover, phytosterols isolated from this unsaponifiable matter and cholesterol were found capable of such activation. The activation of these sterols, purified by physical means, has been accomplished in thin layers of dry substance, in aqueous suspension (110) and in solution in benzene, chloroform (184), ether (53, 220), alcohol (53, 170) and in liquid petrolatum (181). The production of antirachitic activity proceeds with equal rapidity in atmospheres of air (146, 179, 211), in nitrogen (13, 112, 122, 191, 192, 194), or carbon dioxide (122). However, prolonged irradiation of sterols in the presence of air results in destruction of the antirachitic potency (192). Activation has been accomplished at much reduced temperatures (18).

The antirachitic substance so produced loses its activity quickly if kept in crystalline form (173) or in water suspension (122) but when kept in solution in oils, more particularly vegetable oils, its stability resembles that of vitamin D (79, 122). It may be destroyed by heating at 150–200° C. (124). By extraction with anhydrous liquid ammonia the active fraction (probably impure) of irradiated cholesterol was found to make up about 4% of the total and to be effective in preventing rickets in rats on a low phosphorus diet when fed in daily amounts of 2.5 mg. (115). By fractional crystallization of the activated cholesterol from 96% alcohol a substance was obtained after 4 to 6 crystallizations which was soluble in alcohol, non-precipitable by digitonin and capable of preventing rickets in quantities less than 0.5 mg. per 100 Gm. of diet (170, 171).

The rays which produce activation of food materials and sterols containing the provitamin are approximately the same as for prevention of rickets by direct irradiation of the animal (102, 220) but the more efficient rays lie below the upper limit. Heilbron (79) sets the limits as between 250 and 300 $\mu\mu$. The quanta of light of 265 $\mu\mu$ which will produce sufficient vitamin from cholesterol to cause deposition of calcium in the bones of a rachitic rat has been calculated (57).

In attempts to identify the provitamin, numerous derivatives of cholesterol and phytosterol have been irradiated. Negative results have been obtained with oxidation products: such as allocholesterol (194, 260), cholestan-4,7-diol (118, 256), cholestan-4-on-7-al (116, 256), $\alpha$-cholestantriol (206), cholesten (116), $\alpha$-cholesteryl oxide, $\beta$-cholesteryl oxide (116, 256), cholesterol ozonide (116, 256), pseudocholesten (116), cholestenon (116, 256), cholesterilen (116), hydroxycholesterol (256); with hydrogenated derivatives as dihydrocholesterol (104, 102, 122), and dihydrophytosterol (102, 104); and with isomers as $\beta$-cholesterol (116), heterocholesterol (116), $\alpha$-phytosterol (116), $\alpha$-, $\beta$-, and $\gamma$-sitosterol (96), stigmasterol (116, 195). Chlorides (116) and bromides (116) of cholesterol cannot be activated. Of the esters of cholesterol, the acetate (20, 49, 113, 192), isobutyrate (20), benzoate (20, 192) and oleate (124) have been activated; the cinnamate (20), aminacetate (116) and palmitate (48) could not be activated. None of the cholesteryl ethers tested have been capable of activation (20).

The inability to find any derivatives of cholesterol which could be activated by ultraviolet light lead to the discovery that cholesterol which had been purified by chemical means such as preparation of the dibromide and subsequent reduction to cholesterol, was incapable of being reactivated (196). Such cholesterol showed no longer the characteristic absorption spectrum of ordinary cholesterol. From this point coöperative work between Hess in New York, Windaus in Germany, and Rosenheim and Webster in England, and dealing primarily with a study of previous work with its relation to spectroscopic studies resulted in the conclusion that there existed in vegetable oils a "provitamin," which on irradiation with ultraviolet or light of shorter wave-lengths acquired antirachitic activity.

Hess and Weinstock first noted (105) a change in the absorption spectrum of cholesterol during irradiation consisting of decreased absorption (105). Anhydrous cholesterol shows only general absorption (84, 205), ordinary hydrated cholesterol purified by physical means possesses characteristic absorption bands at 293–4 $\mu\mu$, 279–280 $\mu\mu$ and 269 $\mu\mu$ (84). These bands are not shown by cholesterol recrystallized after irradiation (84) and are now known to be characteristic of an impurity which exists to the extent of about $^1/_{60}\%$ (177, 256) and which is probably ergosterol. The absorption spectrum of ergosterol has been recently investigated by several groups of workers (54, 81–86, 120, 163, 166, 167) and found to consist of absorption bands at 270 $\mu\mu$, 281.1 $\mu\mu$ and 293.5 $\mu\mu$ (163). On irradiation, absorption in the region 260–300 $\mu\mu$ disappears and new absorption appears in the region 230–260 $\mu\mu$ with a maximum at 247 $\mu\mu$. On further irradiation this band also disappears. This is in agreement with the disappearance of antirachitic potency following prolonged irradiation and indicates that the absorption band between 230–260 $\mu\mu$ is characteristic of vitamin D. Adam found the absorption spectra of acid extracts of unsaponifiable matter from cod liver oil containing vitamin D and of irradiated ergosterol to be identical (2). In attempts to identify the vitamin, the absorption spectra of several cholesterol derivatives have been determined (85, 86), of which that of cholestenone in alcoholic solution resembles that of vitamin D in that it possesses an absorption band at 243 $\mu\mu$ similar to that of vitamin D at 247 $\mu\mu$ and which disappears rapidly (86).

As a result of these experiments, it is known of the provitamin that: It has three absorption bands with a maximum at about 280 $\mu\mu$ (176, 177) which are destroyed by irradiation with concomitant appearance of antirachitic potency (84, 197).

It occurs with cholesterol and phytosterols, forming with them mixed crystals which are indistinguishable from the materials purified by physical means (256).

It forms with digitonin a digitonide (256), although the vitamin obtained from it does not (197).

It is more readily oxidized than cholesterol being totally destroyed by bromination, oxidation by potassium permanganate, and absorption by charcoal (256, 254).

It behaves chemically, physiologically and spectroscopically like ergosterol (254).

Cholesterol has one double bond in its molecule; phytosterol, sitosterol, fungisterol, etc., two double bonds; and ergosterol alone of the known sterols, three double bonds (182). Ergosterol occurs with fungisterol in ergot oil (43), and in

yeast fat. Its supply is limited at the present time. It has been recently detected in a variety of vegetable oils (79), by means of spectroscopic tests (83), and is presumably present in all oils and food products which have been shown capable of acquiring antirachitic potency on radiation with ultraviolet light. Windaus reports that 35 other sterols have been investigated, none of which showed any antirachitic action on irradiation (255).

Activation of ergosterol has been carried out in alcoholic (14) and in triolein solutions (14, 15) at temperatures of from —180 to +78° (249). It has been brought about by sunlight (198), the cathode ray (138, 140) and by ultraviolet light; the rate of activation increasing in the same order. Activation may also result in the production of fluorescence which is unrelated to antirachitic potency but due to the method of purification of the sterol (190). Various ergosterol derivatives, *i. e.*, dihydroergosterol peroxide (259), ergosterol pinacol, neoergosterol (258), and structurally related compounds as digitaligenin (199) are incapable of activation. However, the ergosterol peroxide can be reduced to ergosterol which is still capable of activation, indicating that it is the true provitamin (259). Doses of irradiated ergosterol necessary to prevent and cure rickets vary from 0.0001 to 0.002 mg. daily (70, 120, 197, 198). Bond has described (21, 23) a color test for the detection of irradiated ergosterol which is dependent on the liberation of iodine from potassium iodide and resulting coloration of starch. As peroxides result from the exposure of a great variety of oils, including mineral oil, to ultraviolet light, this test is not specific for irradiated ergosterol or even for antirachitic substances.

Irradiated ergosterol has been introduced on the market in England and in Germany under the names "Radiostol" (200) and "Vigantol," respectively. These have been used for the prevention and cure of rickets in animals (24, 119, 147, 175, 239) and in children (4, 15, 16, 59, 95, 121, 136, 180, 208, 213, 230, 240, 244, 246, 247). Bond has suggested its use for the treatment of wounds due to the bactericidal effect of its peroxide content (22).

The identification of ergosterol with the provitamin and the conclusion of Hess and Windaus that no antirachitic activation of cholesterol took place after purification through the dibromide has met, however, with some criticism. Jendrassik and Kemenyffi found (135) that fractionation of irradiated cholesterol with ethyl alcohol for three successive times did not remove the activated fraction if irradiation was repeated after each extraction. They were also able to activate cholesterol which has been brominated and reduced. They believe that the provitamin is a conversion product of cholesterol formed in the presence of water, and explain the discrepancy with Windaus' work by the fact that all his work was accomplished in anhydrous solvents. Bills, Honeywell and MacNair have also noted some degree of activability in cholesterol following bromination, which they ascribe either to cholesterol itself or to an undiscovered substance producing absorption bands noted at 135 and 304 $\mu\mu$ (19).

Brief reviews and discussions of this work on the relation between rickets, ultraviolet light and synthetic vitamin production have been published by Hess (92, 93), Hess and Weinstock (107), Heilbron (80), Beumer (12, 17), Komm (143), Vollmer (245) and Edelstein (45).

In addition to the various derivatives and isomers of cholesterol mentioned

above, numerous other compounds have been irradiated with ultraviolet light. Positive results have been obtained with:

Arachnis oil (49, 50, 150)
Bean seed oil (hardened) (40)
Betulin (48, 49)
Brain (94)
Butter fat (21, 248)
Dextrin (slight) (42, 248)
Egg yolk (186)
Excreta (168, 226)
Flour (102, 103, 104, 154, 155, 251, 248)
Hay (222)
Ivory nut oil (50)
Lanolin (110, 111)
Lard (220, 264)
Lemon juice (51, 52)
Lettuce (90, 91, 100, 103)
Linseed oil (88, 89, 91, 101, 103, 106, 248, 251)
Linseed oil (unsaponifiable matter) (108, 109)
Liver meal (slight) (167)
Milk fat (187, 188)
Olive oil (41, 91, 150, 220, 221, 248, 264)
Orange juice (157)
Sawdust (130, 132, 193)
Sesame oil (213)
Skin (55, 90, 102)
Spinach (26, 38, 102, 104)
Sunflower oil (50)
Tissue, muscle (218) lung liver (219)
Vegetables (40)
Wheat (90, 91, 100, 103)
Wheat embryo (48, 248)
Yeast, dried (94, 137) benzene extract (48)

Negative results have been obtained with:

Allyl chaulmoograte (122)
α-Amyral (116)
Apocholic acid (116)
Calcium lactate—ferric citrate (251)
Carrots (90)
Casein (40, 248)
Chlorophyl (103)
Citonella oil (102, 104)
Cocoanut oil (old) (220)
Corn (unground) (167)
Corn oil (hydrogenated) (251)
Cymene (102, 104)
Dextri-maltose (248)
Egg phosphatide (102, 103, 104)
Eosin (248)
Ether (227)
Gelatin (248)
Gluten (wheat) (248)
Glycerol (103)
Hemoglobin (103)
Hydroquinone (227)
Iron (reduced) (248)
Lecithin (141)
Linseed oil (saponifiable matter) (108)
Mineral oil (88, 91, 106, 220)
Oleic acid (102, 104, 141)
Paraffins (227)
Phloroglucin (227)
Protein (42, 227)
Red blood cells (103)
Salt mixtures (248)
Stearic acid (141)
Sugar (65, 248)
Water (distilled) (91)

It has been noted repeatedly that while fresh samples of certain vegetable oils acquire antirachitic activity on exposure to ultraviolet light, that old samples of the same oils cannot be activated. This has been demonstrated for cocoanut oil (93, 220), corn oil (42, 88, 91, 220), cottonseed oil (99, 106, 155, 220), oleo oil (220), peanut oil (189, 220). Starch has been reported both capable (42) and incapable (40) of activation. This undoubtedly depends upon the source of the starch and the degree of purity. Waltner has reported that tyrosine could be activated (248). This has been denied (141, 144).

The exposure of cod liver oil to ultraviolet irradiation results in disappearance of its normal fluorescence (1, 174) and various other changes in physical properties (1). Attempts to strengthen the oil by such irradiation in the presence of air resulted in the discovery that the antirachitic potency was not increased by brief irradiation (32, 261, 262) and in some cases was apparently decreased by more

extended exposure (1, 94, 262). Moreover, such irradiation in air may result in serious destruction of vitamin A (1, 253). Work done in the Squibb Laboratories indicates that no change in either vitamin A or D potency takes place on irradiation of cod liver oil in vacuo. Stoeltzner has claimed that the ergosterol present in cod liver oil may be activated by the addition of yellow phosphorus (228). This has not been confirmed. Cod liver oil has, however, been fortified by the addition of irradiated cholesterol (94, 173).

Exposure of lactating animals (56, 66, 126, 223) and women (114) to ultraviolet light has been shown to increase the antirachitic potency of their milk. Milk may also be exposed to irradiation with resulting increase in its potency. This is usually done by exposure of a thin layer at a distance of about 2 ft. (33, 236) from a quartz mercury vapor lamp for a period of 45 sec. (75) to $^1/_2$ hr. (33). It is likely to undergo, especially in the presence of air, a deterioration in taste probably due to oxidation of its protein (207) which is for that reason sometimes removed. Irradiation in air leads to a destruction of vitamin A (38, 234, 236) and the process is carried out by Scheer in an atmosphere of carbon dioxide (201, 202).

Dried milk has also been irradiated with resultant increase in antirachitic potency. A layer of 1 to 2 mm. in thickness (44, 69) is exposed to the lamp at a distance of about 1 ft. (44) [30 cm. (69)] for a period varying from 2 min. (44) to 1 hr. (69). Dow and Supplee have reported that no destruction of vitamin A (233) or C (231) occurs except with prolonged exposure. They have increased the calcifying properties of both summer- and winter-produced milk by irradiation (232). Irradiated milk has been used to some extent in the prevention of rickets (2, 31, 35, 71, 145). In Germany, various other irradiated materials, *i. e.*, protein-free butter fat (187, 188); plasmon (a casein-fat preparation) (65) gruels (71) and "Carnolactin" (milk-beef preparation) (74) have been used clinically.

These clinical experiments with irradiated cholesterol (97, 108), ergosterol (119, 148, 238) and milk (145) have shown that the synthetic vitamin has effects on calcification and on the calcium and phosphorus metabolism identical with those of the antirachitic vitamin of codliver oil.

The ultraviolet light for the above work (30, 220) has been obtained from sunlight, and various artificial sources such as the open carbon arc (220), the iron arc (220), and the mercury vapor lamps. Ordinary Mazda bulbs (127) emit some of the active light rays as does also Wood's light (166). The majority of the work has been done with Cooper-Hewitt Uviarc lamps with various types of burners. The Hanovia, Burdich, Hanot and Heraeus lamps have also been used. The spectra of the quartz mercury vapor lamps extends from 1850 to 14,000 Å. The ultraviolet spectra of the Hanovia (47) and of the Uviarc lamps (181) do not differ markedly. The total radiation grows rapidly with increase of voltage and depends greatly on the degree of cooling of the lamp. The intensities of the infra-red and ultraviolet grow the fastest. The energy characteristics are affected also by the dimensions of the lamp. The falling off of efficiency with age, due to vitrification and discoloration of the quartz, is not marked in the extreme ultraviolet (181). The intensity of the total radiation, as well as of the ultraviolet component, decreases to about one-half to one-third of its initial value in the course of 1000 to 1500 hours. During the first 500 hours' usage, no marked difference was observed in the proportion of ultraviolet emitted by the two types of lamps (47). The spec-

tral range of the mercury vapor lamps is discussed by Coblentz (28). Various methods of standardizing the intensity of the radiation have been proposed (5, 10, 60, 61, 142, 164, 165, 179, 252).

When it is desired to use only light of a limited wave-length, the rays are passed through suitable filters which cut out all light of other wave-lengths. These filters may consist of solutions of dyes, of gelatine films or of glass. Wratten Light Filters (gelatin) are sold by the Eastman Kodak Co., and glass filters by the Corning Glass Co., American Optical Co., Bausch & Lomb Optical Co., etc. The absorption spectra of some of these are given by Ellis (47) and the Bureau of Standards has determined the absorption spectra of a large number of glass filters (Tech. Paper 119, 148). The use of filters has been discussed to some extent by Hess and Weinstock (98, 104, 105).

Patents covering the production of vitamin D in foods and other products by irradiation methods have been granted to Goodall (64), Harriman (77), Jaeger (134), Merck (158, 159, 160, 161), Scheidt (203), Spolverini (215), Steenbock (217), Stamso (216) and Tillisch (235).

Knudson and Coolidge found (139) that exposure of rats on a rachitic diet to high voltage cathode rays did not protect from rickets in the largest doses possible on account of severe action on the animal tissues. However, they were able to activate by this means cholesterol which protected from rickets when subsequently fed to rats (139). Yeast, starch, cottonseed oil (138), and ergosterol (140) have also been activated. The minimum curative dosages for rats of ergosterol, irradiated by ultraviolet and cathode rays were 0.00002 mg. and 0.0025 mg. daily, respectively. Evidently, then, ultraviolet exposure produces more potent products than cathode ray exposure (140).

Exposure of cholesterol to Roentgen rays results first in appearance of photoactivity (76), followed by chemical change (183), oxidation (185) and destruction, especially when dissolved in chloroform, bromoform and carbon tetrachloride (36, 37). Roentgen rays produce no change in the spectrum of pure ergosterol (162) thus indicating lack of activation. Spectroscopic and biological examination of ergosterol irradiated successively by ultraviolet and Roentgen rays shows that the latter have a destructive action on vitamin D (162). It has been reported that foods irradiated with Roentgen rays are toxic as the result of vitamin destruction (67).

Closely related with the development of antirachitic potency in oils by irradiation with ultraviolet light, especially when carried out in air, is the phenomenon of photoactivity. In 1924, Hume and Smith performed some experiments which led them to state that ultraviolet irradiation of air in jars impressed on it some property which promoted increased growth in rats subsequently inhabiting those jars when fed a diet deficient in fat-soluble vitamins. This was subsequently corrected by the above authors (130) who traced the growth-promoting substance to sawdust present in the jar during irradiation; and by negative results obtained in attempts to prevent rickets in growing chicks with irradiated air (125). Air which had been

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NOTE: Since presentation of this paper United States Patents covering irradiation methods for the production of vitamin D have been granted Steenbock (1,680,818), Pacini (1,681,120) and Chesney (1,704,173). A patent is pending on the use of the cathode ray for the same purpose.

ionized by exposure to emanations from radium bromide (27) and water containing radium bromide or ozone (106) were likewise incapable of preventing rickets in animals.

Almost simultaneously with the first reports of Hume and Smith, Kugelmass and McQuarrie observed that substances curative of rickets when oxidized (by oxygen or spontaneous autoxidation by air) produced a definite blackening of a photographic plate when screened by quartz but not by glass and concluded that ultraviolet rays were produced on oxidation (149). Similar observations have been made by others (7, 29, 78, 151, 169, 229, 241, 242, 243) especially after ultraviolet irradiation, but with the exception of Kugelmass and McQuarrie, these believed it to be due to chemical effects produced in the irradiated substance. No photographic effect could be noted on using an air-tight camera (34). Carrick has investigated the effect of exposure to irradiated cod liver oil in the development of experimental rickets in chicks (25).

Ordinary cod liver oil is photoactive (87, 241) and becomes more so on irradiation (242). The photoactivity of such irradiated substances has been ascribed to the phosphorescence of the quartz (21), to the "Russell" effect (78), or to ozone (151, 229) or hydrogen peroxide (243), organic peroxides (73) and ozonides (243). According to Vollmer and Serebrijski (243) all antirachitic materials contain photoactive substances. The photoactivity of cod liver oil is destroyed by boiling (73, 87); is increased by heating to 100° C. (87) and by exposure to sunlight (73) or to ultraviolet light (241, 263) in air or oxygen; and is not proportional to antirachitic potency (263, 7). The same facts are true of induced photoactivity of cholesterol (229). The photoactivity of various oils and other compounds both before and after irradiation has been investigated (7, 73, 78, 151, 169, 241, 242, 243, 263).

Similar investigation of the prevention of rickets in animals by exposure to irradiated sawdust has shown it to be due, not to secondary radiations (132, 152) as this photoactivity is likewise the result of a chemical fog (152) presumably peroxide (243), but to the presence therein of sterols which acquire antirachitic potency on irradiation (93).

The results of extensive work done on this problem indicate that the origin of naturally occurring antirachitic vitamin is based on the ultraviolet rays present in sunlight. Sunlight has been shown necessary for the formation of the vitamin in plant tissues (30). Tisdall has argued (237) that the vitamin produced by action of sunlight on sterols in vegetable matter and subsequently consumed by small fish is the source of antirachitic potency in cod liver oil. Although our knowledge of the production and properties of this vitamin has been greatly extended during the past few years, we as yet know little of its chemical nature. It is the opinion of Baly (6) that a vitamin is a chemical substance, which may be already known, in a state of high energy content. Since ultraviolet light is a source of energy, the recent knowledge concerning the synthesis of vitamine D seems to support Prof. Baly's views.

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# 125TH ANNIVERSARY OF THE DISCOVERY OF MORPHINE BY SERTÜRNER.*

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When it is recalled that the practice of medicine is practically impossible without morphine, that directly or indirectly morphine has promoted scientific discovery in medicine, that morphine led in the development of pharmaceutical chemistry and of experimental pharmacology, and hence of rational therapeutics, the significance to Medicine of Sertürner's achievement 125 years ago becomes apparent. From the fact that morphine has been the sovereign pain-killer during these past 125 years, the humanitarian side of Sertürner's discovery achieves distinction. Yet, if one is to judge from the scanty mention of the subject in the literature of medicine, the significance of Sertürner and his achievement has been relegated to almost complete obscurity.

Fig. 1.—Friedrich Wilhelm Adam Sertürner, 1783–1841.

It is probably true that alongside of such glorified products as the endocrines, the vitamines and the synthetic medicinals, the isolation of morphine was a comparatively humble achievement. It required no munificent grant, no extensive laboratory equipment, no highly organized institute or factory; in fact, it required nothing but the ordinary equipment of a pharmacy and the self-determination of a man. Nevertheless, there is a charm, if not a lesson, in the very simplicity and the directness of this signal achievement.

In presenting this résumé on Sertürner and his achievement, I venture to recall the circumstances attendant upon the discovery of the first alkaloid, and to refresh our memories of the obscure pharmacist of Paderborn, who achieved by his own unaided efforts. The discovery of morphine was no insignificant event in Sertürner's day, and its significance has not diminished in importance during a lapse of 125 years, which merely testifies to its permanence and should excite both our curiosity and admiration. In Germany, the worthiness of Sertürner and his achievement had already been recognized, and recently again attention has been drawn to the subject by Dr. H. Coenen, Dean of the Medical Faculty, and Prof. H. Freund, professor of pharmacology, in the University of Münster; but in other countries, including our own, notice of the event has been conspicuous by its absence. This, therefore, may serve as an additional reason for this presentation.

* Read before the Medical History Society of the University of Oregon Medical School, Portland, Oregon, January 11, 1929.

BIOGRAPHICAL.

Friedrich Wilhelm Adam Sertürner (Fig. 1) was born in Neuhaus near Paderborn, Germany, June 19, 1783 (Fig. 2). He was apprenticed at 16 years of age to the Royal Pharmacist Cramer at Paderborn and there (Fig. 3) he discovered morphine in 1803 at the age of 20 years. To Cramer, his preceptor, he dedicated 25 years later his newly founded "Annalen."

The details of Sertürner's personal life are scant, but apparently he was of Italian or French descent, the original family name being Serdinier, from Sardinia. His education appears to have been limited, about average for a boy of his station; but he proved himself a worthy apprentice. It appears that he was rather imaginative, this quality being tempered with practical common sense. In later years he become a hypochondriac, had gout, and led a miserable existence, being fully aware of the great benefits his discovery conferred on humanity. He was a

Fig. 2.—Sertürner's birth-place at Neuhaus, Westphalia, Germany. Proposed Museum.

Fig. 3.—Cramer's Pharmacy at Paderborn, where Sertürner discovered Morphine, in 1803.

man of noble character, a patriotic and charitable citizen. Sertürner died at the early age of 57 years in Hameln on February 20, 1841, an unhappy and ridiculed man. Nolte (*Archiv der Pharmazie*, 4, 29 (1842), 1), states that his death occurred after taking a second cup of tea with his family. He had suffered from convulsions (uremic?) shortly before death. The cause of the sudden death was ascribed to "a gush of water into the spinal canal and infiltration of water into the brain" (apoplexy?). In 1917, 76 years after Sertürner's death, Prof. Stich of Leipzig identified Sertrüner's casket in the family grave in Bartholomew's Chapel at Einbeck. This event undoubtedly stimulated further recognition of Sertürner in his own country. In 1921, or 80 years after his death, there appeared on the German emergency notes (Fig. 4) of that year a picture of Sertürner's birth-place and his portrait with these words;

"Deine Hütte verfallen, Dein Grab verwest,
Dein Werk wird bleiben, so lange die Erde steht."

In Cramer's pharmacy at Paderborn, a memorial tablet has been placed with this inscription: "In diesem Hause entdeckte 1803 Fr. W. Sertürner das Morphium." This tablet was unveiled in 1921, or 118 years after the discovery. Another memorial tablet was unveiled for Sertürner at Hameln in 1905 by the president of the German Pharmaceutical Society, and a plaque was placed on the Pharmacological Institute of the University of Münster in 1928 (Fig. 5).

### SERTÜRNER'S EARLIEST RESULTS ON THE CONSTITUENTS OF OPIUM.

The first announcement of Sertürner's work with opium was in 1805, in Trommsdorff's *Journal der Pharmacie*, Vol. 13; at this time he described his discovery of meconic acid in two letters to the editor. There are no indications in these letters when he began working on opium, but he states that he had made observations before Derosne whose work had been reported in the *Journal der Pharmacie*, 12, (1804). From this it may be inferred that he had done work in 1803, and, in support of this inference, there is an intimation in his paper of 1817 to the effect that he made a successful isolation of the alkaloid in 1803. This date has been generally accepted as the date of the discovery.

Fig. 4.—Two-mark German emergency note of 1921, commemorating Sertürner, the Discoverer of Morphine.

In 1806, in Vol. 14 of the same *Journal*, he described the results of 57 experiments, detailed over 48 pages, with both opium acid and with a new substance which caused sleep and was morphine. Sertürner called it the "*Principium somniferum*" of opium. This paper has the appearance of a finished contribution although the 57 experiments are not really individual experimental trials, but merely successive steps in a relatively few experiments. The first 25 experiments may have been done early, perhaps in 1803, with the simple reagents that could be had in the drug store.

In these early experiments, all of which were carried out in Cramer's Pharmacy at Paderborn, Sertürner's most important reagent was ammonia. His object was to correct the irregular therapeutic results with the opium extracts used by the physicians of his day. It was an important problem. The chemical part of his work with the drug at this time (1803) was somewhat peculiar and quaint, but he made rather interesting and crucial experiments, the results of which encouraged him to pursue the subject. For those times the experiments were epoch-making. For one thing, he conceived of isolating the active constituent of a medicinal plant, then only a theoretical possibility; but Sertrüner actually obtained results. He made experiments on 4 dogs with extracts before and after alkalization, and also with pure crystals, noting especially the narcotic effects. He found that, when the basic constituent of opium was removed by precipitation with ammonia and by filtration, the extracts did not cause narcosis in dogs. Hence, he believed that there was something important in the basic precipitate of the plant extract. Obviously, Sertürner confirmed his suspicion by animal experimentation, and thus, he was an early exponent of experimental pharmacology. In fact, he preceded by

53 years the founding of the first laboratory of experimental pharmacology by Buchheim (1856) in Dorpat, Russia (to-day, Tartu-Dorpat, Esthonia). Sertürner also tested the odoriferous portion of the extracts on a mouse and found it was inactive on inhalation over long periods. In the 53rd experiment, he summarized the constituents of opium as follows:

"Extractive with gummy portions, balsam-like matter, narcotic principle, mohn acid (opium acid), resin, gluten, rubber, calcium sulphate, aluminium silicate (earth), volatile odoriferous constituent, which appears to be composed mostly of hardened plant protein, fibres and impurities."

In the paper of 1806, Sertürner drew definite conclusions. These were that the great activity of opium was not due to the resin and extractive, but to the crystalline constituent, which he designated the narcotic constituent as against the current hypothetical narcotic substance; and that it was improbable the odoriferous

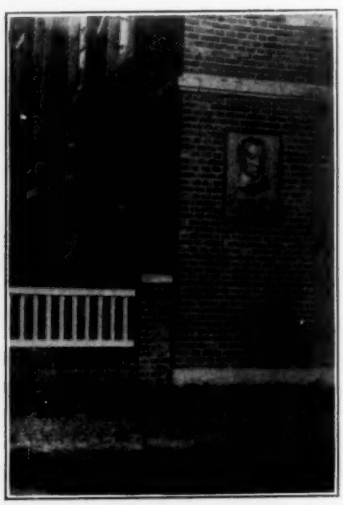

Fig. 5.—Plaque in honor of Sertürner on the Pharmacological Institute, University of Münster.

Fig. 6.—Present Pharmacy at Einbeck, formerly Sertürner's Pharmacy in 1809–1820.

constituent and resinous extractives possessed medicinal virtues. He recommended the use of strong alcohol as the choice menstruum for opium instead of weak alcohol or water; for, by so doing, physicians would no longer get irregular results with opium. Sertürner concluded further that his work gave new light on the action of opium, but that it would have to await the final decision of physicians. This indeed was a healthy attitude for the therapeutics of his day, and could with advantage be emulated to-day. The editor (Trommsdorff) of the *Journal* appended a note stating that the experiments reported by Sertürner contained many interesting suggestions for which the chemical public was much indebted. However, he warned that there had been so many pieces of work on opium that one should not regard the matter closed, and he hoped the new claims would be further investigated and many obscure features elucidated.

Sertürner now (in 1806) left Paderborn and established himself at Einbeck where from 1811 to 1817 he continued the work with opium in his own laboratory

(Fig. 6). His later papers were published from Einbeck. Two papers appearing in 1817 are important; for, in these, Sertürner gives the details of his method of isolating morphine and meconic acid and fully describes their physical and chemical properties and actions on man and animals. The details are as interesting as are the methods he employed.

SERTÜRNER'S METHOD OF ISOLATING, AND RESULTS WITH, MORPHINE IN 1817.

Sertürner prefaced this paper by stating that the Parisian pharmacist, M. Derosne, undertook the isolation of the constituent 14 years prior to the time of his first successful isolation of morphine, but their results were so different and contradictory that the problem remained as dark as ever. He stated further that his original contribution went unnoticed; that it had been quickly gotten together and the quantity of morphine he had worked with was too small, and some could not repeat his results. In this paper Sertürner stated that he desired to present science not only with a remarkable plant constituent, but also with the discovery of a new alkaline principle (basic).

Gilbert, the editor of the *Annalen der Physik*, criticized the paper in a long foot-note, justifying himself for accepting Sertürner's somewhat un-chemical paper, and stating that Sertürner apparently overlooked the work of Thénard and Chevreul, who had previously found that acids unite with many plant constituents to form true compounds, and advised Sertürner to study this work. Gilbert said further, that, if Sertürner's body from opium—his morphine—was a true plant constituent and consisted of carbon, hydrogen and oxygen, the chemists had something to learn from this plant constituent in being a base, as claimed, and behaving like an alkaline earth. Gilbert thought that morphine could be a base without being an alkaline earth. It appears that no one recognized the importance of the nitrogen in the morphine as being the real clue to the basicity, although Sertürner claimed he found this element occasionally.

*Details of the Method and Results.*—Eight ounces of dry opium were repeatedly extracted with small portions of distilled water until the extracts remained colorless. The combined extracts were clear, but, on addition of more water, precipitation occurred and the precipitate redissolved with more water. The watery extract was now supersaturated with ammonia. Crystals appeared and these were washed with water until clean; they consisted of morphine. Some extractive and meconic acid adhered to the morphine. The total yield of crystals was 16 drachms, or about 25 per cent. The crystals were next treated with dilute sulphuric acid, precipitated again with ammonia, and the newly-formed dry crystals were rubbed with alcohol and dissolved. This treatment left much brown extractive behind. The yield now was 8 drachms, or about 12.5 per cent. The morphine was next dissolved in alcohol, and allowed to re-crystallize, this process being repeated several times to purify the product. The final crystals were parallelopipeds, while Derosne's crystals were prismatic and gave a strong red color with iron.

The properties of Sertürner's pure morphine were as follows: It was colorless, slowly and slightly soluble in boiling water and easily soluble in alcohol and ether. Its taste was bitter. It turned red litmus blue, and turmeric, brown. There was no ammonia in the crystals, which were soluble in acids with neutral reaction and formed the bicarbonate, sulphate, hydrochloride, nitrate, meconate, acetate and

tartrate salts, all of which were prepared by Sertürner. Elementary analysis showed the crystals contained carbon, hydrogen and oxygen, and perhaps nitrogen. The crystals were easily oxidized and melted at a low temperature. Sertürner stated he employed a competent chemist to help him with the elementary analysis. Obviously, Sertürner had described all properties of morphine correctly, except that he did not establish its nitrogen content.

*Actions on Human Body.*—Sertürner used three young men as subjects, and described his own sensations after taking $^1/_2$-gr. doses of the pure crystals, each dose being taken in $^1/_2$-fluid drachm of alcohol and several ounces of water. He warned against taking the drug by mouth, unless dissolved in alcohol or little acid, because he thought it would not be dissolved in the gastric juice and absorbed. Sertürner described the symptoms as follows: after the first $^1/_2$-gr. dose, there were facial redness and apparent increased body activity; after the second $^1/_2$-gr. dose, one-half hour later, the previous states were increased and there were nausea, dullness in the head and general numbness; after the third $^1/_2$-gr. dose a quarter of an hour later, depression was marked, and there were loss of power, general numbness, narcosis, with a dreamy state, and small spasms in the legs and arms which coincided with the pulse beats. The latter effects Sertürner declared to be poisoning, and he concluded that the drug was very effective in small doses. He concluded further that, *since no other constituent of opium produced these peculiar actions of narcosis, etc., the valuable medicinal properties of the drug opium were due to the morphine.* Sertürner added that the morphine abolished toothache. At this time (1817), he named his product *Morphine,* from *Morpheus,* the *God of Sleep.* Thus was Sertürner remarkably correct in his description of the narcotic and analgesic actions of the newly-discovered morphine.

In the appendix of the same paper, Sertürner described an improved method for isolating morphine. He now advised rubbing 8 ounces of opium with 2 to 3 ounces of acetic acid and some distilled water, the whole to be diluted with 2 or 3 pounds of cold water and strained. The slightly colored extract contained morphine acetate and opiate. The morphine was then precipitated with ammonia; the mixture was concentrated somewhat and filtered to separate the morphine crystals, which were then treated with barium acetate. This treatment gave morphine acetate and barium opiate, the latter a precipitate, which was filtered off. In this way, Sertürner claimed, the morphine was obtained pure.

*Meconic Acid.*—In the same year (1817), Sertürner published another paper in Vol. 57 of Gilbert's *Annalen,* the object being to describe what he called "Eine der fürchterlichsten Gifte der Pflanzenwelt" (one of the most horrible poisons of the plant kingdom), referring to meconic acid, which he now compared and contrasted with morphine. He stated that morphine, in small doses, gave an agreeable sensation and sleep, while meconic acid caused poisoning in every man, being dangerous to life. Previously he had held that meconic acid was harmless, but now he wanted this impression corrected, saying that it belonged to the most terrible poisons. His evidence was as follows: 3 grs. of sodium meconate given to a dog by mouth caused vomiting, loss of leg control, paralysis of hind legs, and deepened and slowed respiration. Eventually, weak spasms occurred and there was a "feeling of anxiety," but the dog recovered. Sertürner himself took $^1/_{10}$ gr. and experienced the "feeling of great anxiety." A dog was given 1 gr. of barium

meconate with resulting increased excitability, emesis and expulsion of tapeworms.

From this evidence Sertürner concluded that meconate acted oppositely to morphine. We know now that many of the effects of meconate described by Sertürner occur also with morphine. Many physicians reported to him that meconate was ineffective as analgesic in toothache and cramps, while morphine was effective. Moreover, he observed that roosters and cats did not react to meconate, and also that 10 grs. of opium administered to a rooster gave no results. Another difference cited by Sertürner was, that meconate gave a deep color with iron while morphine did not; it gives a blue color. He concluded this paper by pointing out that morphine was a base of the plant and had the advantage over opium in that the meconate of the latter was harmful to animal life. Thus, by isolating morphine, the purified substance was free from the injurious one. He made the deduction that it was characteristic of all products of the animal kingdom to be basic in nature whereas those of plants were acid, *i. e.*, in combination with acid, as was morphine in opium. The latter was a fairly clever distinction for that time, although it would not be accepted now.

In commenting on Sertürner's work, Robiquet stated that the surprising thing to chemists was that morphine should be an alkali, *i. e.*, a base, and that the opium extracts should be acid. From this, Robiquet inferred that the morphine of the opium extract was in the form of a salt, which, on alkalinization, liberated the base, but he questioned Sertürner's contention that morphine existed in opium as morphine meconate. Nevertheless, Sertürner called morphine the correct thing and recognized an important property of alkaloids, *viz.*, their basicity; he showed also that alkaloids did not exist as bases in plants, but in combination with acid radicles.

### PRIORITY OF DISCOVERY OF MORPHINE ("SEL DE DEROSNE").

Sometimes the priority of the discovery of morphine has been ascribed to the French pharmacist, Derosne, who used alcohol to extract opium. Derosne's extracts at best were crude extracts and contained besides morphine all the other constituents of opium. "*Sel de Derosne*" was the name of the crude extract. Sertürner did not believe Derosne had isolated morphine. He proved that isolation was only possible by making the extract alkaline first, and showed that the resulting precipitate, and not the supernatant fluid, caused narcosis. Derosne employed neither of these steps. Derosne's contemporaries at the Institut de France settled the matter by voting a prize of 2000 francs to Sertürner instead of to their countryman. The prize was voted to Sertürner for having recognized the basic nature of morphine and for having discovered a method which had produced great medical discoveries.

*Recognition of Sertürner's Work.*—The Institut's recognition did not come before Gay-Lussac's opinion. Gay-Lussac read a French translation of Sertürner's work in the *Annales de Chimie*, 5 (1817), 121 and expressed surprise that the extremely important discovery in Germany had remained unnoticed in other countries. In that year the University of Jena conferred the degree of Doctor of Philosophy on Sertürner and he was elected to membership in scientific societies in Marburg, Berlin, Paris, Batavia, St. Petersburg and Lisbon.

SERTÜRNER'S LATER WORK AND DECLINE.

The year 1817 was undoubtedly the high point of Sertürner's scientific career; after that came the decline. It was in the short space of 14 years (between 1803 and 1817), and between the ages of 20 and 34, that Sertürner did his best work. After the discovery of morphine, he busied himself with numerous things. In fact, his energies were too diffuse. He was a many-sided man of a restless, impatient, and perhaps impulsive, nature. He seemed somewhat impatient with the chemists of his time, accusing them of lack of vision and of interest in practical problems, but unfortunately he himself became merely an arm-chair critic. This was quite in contrast with his early life. Many of his later ideas had been nourished from his earliest work with opium.

Among various items, which very early claimed his attention, were questions of benzoic acid in fennel water, nitrate, active constituents of drugs, animal charcoal, borax, nut-galls, tannins and explosives. In 1838, he tells of experimental work which had occupied his attention from youth on. From the results obtained he held that the caustic alkalies (hydrates), then as yet regarded as elementary substances, were composed of oxygen and a metallic element similar to hydrogen. This conception was ridiculed by Gehlen to whom he had sent his manuscript in 1806; and shortly thereafter, Davy announced his discovery of the same thing in another way.

In Sertürner's time terrible epidemics of cholera raged in European countries and he directed his thoughts to the control of this scourge. He pleaded with scientific men of his day to give attention to this all important problem. He anticipated Koch in the matter of treatment, though without knowing the rational basis. Sertürner conceived of cholera as a gastric disturbance and was supported in this by an English physician, Henderson. Together they proposed to cure cholera with magnesium oxide, castor oil and laudanum. One reason for the choice of magnesia was the reported presence of acetic acid in the mouth and rectum of dying victims. The other reason was an assumed benefit from alkaline earths in disease in general. The proposed remedy was never put to a test. Sertürner's most important advice for the prevention of cholera was to purify (boil) the drinking water, and fifty-three years later Koch discovered the cause and confirmed Sertürner's hunch on the preventive measure.

Nolte has discussed at length Sertürner's conceptions of body functions and diseases. Most of these conceptions were erroneous; for example, he proposed to use alkali earths in the treatment of nearly all diseases just as he explained body processes on the basis of changes in alkaline earths. It might be contended that he was not far from the truth about physiological and disease processes. For, does not modern physiology recognize the importance of a proper acid-base equilibrium for health and medicine, the disturbances in this equilibrium for disease, *viz.*, the clinical acidosis of the dysenteries, cholera, etc.?

During this period Sertürner founded a system of Chemical Physics (modern Physical Chemistry). He also founded, and published during three years, the "*Annalen für Universalsystem der Elemente.*" In these publications he discussed the life element "Zoön," the cold nature of light, atmospheric heat, various drugs, the art of gunnery and many other things, all of which were speculative. He

began to show his weakness, and for all these things he was ridiculed and attacked. He complained in his *Annalen*, saying, "As a result of my work with opium, von Sternberg called me a pupil and later another distinguished German chemist called me a quack." In his necrology of Sertürner, Buchner said, "Sertürner made a notable beginning in the realms of Chemistry and Pharmacy, and indicated the greatest hopes, but he failed to realize a beautiful and fruitful promise because of his speculations in physics and medicine and of his controversies."

### VALUE OF SERTÜRNER'S ORIGINAL WORK.

There is no doubt that Sertürner was not a well-read or scientifically trained man, but that makes his work and conclusions all the more remarkable. Considering this lack of training he possessed the power of making remarkably correct deductions. His discovery of morphine was accomplished rather simply and cleverly, in fact, under exceedingly humble circumstances. He worked intuitively and later became a speculative philosopher. To-day he might be regarded as a man of "good hunches." He worked alone, and, instead of being given advice, was showered with rebuke and bitter criticism. He was reproached for not being more scientific, though his critics were no supermen; some did not accomplish as much as he, but, secretly, made use of much that Sertürner discovered.

There is no doubt that Sertürner laid the foundation of alkaloidal chemistry. After his discovery and the isolation of morphine, came the following important alkaloids; emetine (Pelletier and Magendie, 1817), strychnine (Pelletier and Caventou, 1817), quinine (Pelletier and Caventou, 1820), caffeine (Runge, 1820), atropine (Mein, 1833), aconitine (v. Planta, 1850), veratrine (Merck, 1855), cocaine (Wöhler, 1860), eserine (Jobst and Hesse, 1864), muscarine (Schmiedeberg and Koppe, 1870), pilocarpine (Hardy, 1875), pelletierine (Tanret, 1878), nicotine (Liversedge, 1881), ephedrine (Nagai, 1887) and ergotoxine (Barger and Carr, 1906). Accordingly, a span of 103 years elapsed before the isolation of these 15 alkaloids was accomplished. These discoveries were for the greater part only repetitions of what the obscure Paderbornian pharmacist had done under difficulties. He recognized the principles which govern the isolation of these important plant constituents. In fact, his work was the starting point for the discovery of all active constituents, which were destined to play an important rôle in the development of experimental pharmacology and of rational therapeutics. For it is only by using definite and pure constituents that accurate doses can be given and their effects scientifically studied. His discovery came at the zenith of the nihilistic period in therapeutics, and thus served as a starting point for the period of reconstruction which followed and still continues.

Besides isolating morphine, as the first alkaloid, Sertürner determined its chemical nature and showed that the effect of opium on man was essentially due to this constituent. His work has been amply confirmed and has stood the test of time, but it cannot be said that it has been greatly extended along chemical lines. For instance, the structural formula of this most important alkaloid has not been definitely established; nor has the alkaloid been synthesized. These deficiencies exist despite the tremendous resources of present-day chemistry.

Humanity owes Sertürner a permanent debt of gratitude for his contribution to the alleviation of suffering. His discovery is not limited in application to one

disease as is insulin to diabetes or diphtheria antitoxin to diphtheria, but it is widely applicable to the relief of that distressing symptom—pain—in all kinds of conditions. As a matter of fact there is hardly a branch of medicine which is not indebted to Sertürner's discovery for making it possible to serve mankind. This beneficence extends even to animals of the lower orders. Considering that this discovery led directly to the discovery of such important alkaloids as quinine, cocaine, emetine, ephedrine and others, it is not too much to say that Sertürner promoted not only the conquest of pain, but also of disease prevention, and thus facilitated the conquest of continents and of uncivilized peoples. Thus, Sertürner's discovery stands well alongside of the greatest discoveries which have benefited the human race. No wonder that it was hailed as an important one.

Now, on the 125th anniversary of this important discovery, we reaffirm our gratefulness for the timely effort and native talent of the once obscure pharmacist of Paderborn. There is indeed a lesson in his achievement. In it we have an example of drug store research 125 years ago. Would it be too much to expect of American Pharmacy to draw a fresh inspiration for higher and better things from Sertürner and his discovery? Could this happen, it would contribute to her a life element of inestimable worth.

AUTHOR'S NOTE: My acknowledgments are due to the University of Wisconsin Library, Madison, Wisconsin, for a loan of the journals containing the papers by Sertürner; and to Prof. Dr. H. Freund of the University of Münster, Germany, for certain cuts, which have been used in this paper, and a pamphlet by Dr. Krömeke, previously unknown to me, all of which were received after completion of this paper.

REFERENCES TO RECENT LITERATURE.

(1) H. Coenen: *Med. Klinik*, 24 (1928), 357.
(2) H. Freund: *Ibid.*, 24 (1928), 398.
(3) F. Krömeke: Friedrich Wilhelm Sertürner, der Entdecker des Morphiums. Lebensbild und Neudruck der Original, Morphiumarbeiten. Gustav Fischer, Jena (1925), 93. This contains a biographical sketch by Dr. Krömeke, with references to older literature on Sertürner, and reprints of the five papers on opium and morphine by Sertürner.

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# SYRUP OF FERROUS IODIDE AND THE OFFICIAL HYDRIODIC PREPARATIONS.

BY H. V. ARNY, BENJAMIN VENER AND LESLIE C. JAYNE.

(*Concluded from p. 268, March Issue*).

## *Part II.*

### SYRUP OF FERROUS IODIDE.

(Work performed with Leslie C. Jayne, Ph.Ch., B.S.)

Three samples of this syrup were prepared:

*A.* Exactly as directed by U. S. P. X. The fresh sample assayed 5.1793 per cent ferrous iodide.

*B.* As directed by U. S. P. X with omission, however, of the hypophosphorous acid. The fresh sample assayed 5.4116 per cent ferrous iodide.

*C.* As directed by U. S. P. X except that the sugar is replaced by the same

amount of invert sugar.[1] The fresh sample assayed 5.0942 per cent, of ferrous iodide.

TABLE VII.

SAMPLE A. SUCCESSIVE ASSAYS OF SAME SAMPLE STORED IN 2 ONE-PINT BOTTLES. UNDER "REMARKS" MENTION IS MADE AS TO WHETHER THE ASSAYED SAMPLE WAS TAKEN FROM THE FULL OR PARTLY FULL BOTTLE.

| Date. | Age. | Color. | Scum. | Free iodine. | % $FeI_2$. | Remarks. |
|---|---|---|---|---|---|---|
| 10–26–26 | .... | Green | ..... | ... | 5.1793 | Partly filled pint bottle |
| 11–27–26 | 1 mo. | Green | ..... | ... | 5.1793 | Full pint bottle |
| 12–28–26 | 2 mos. | Green | ..... | ... | 5.1793 | Full pint bottle |
| 2– 1–27 | 3 mos. | Green | ..... | ... | 5.1407 | Full pint bottle |
| 3– 3–27 | 4 mos. | Green | ..... | ... | 5.1793 | Full pint bottle |
| 4– 9–27 | 5 mos. | Green | ..... | ... | 5.1793 | Full pint bottle |
| 5–23–27 | 6 mos. | Green (cloudy) | Present | ... | 5.249 | Full pint bottle |
| 6–25–27 | 7 mos. | Green (cloudy) | ..... | ... | 5.1793 | Full pint bottle |
| 9–20–27 | 10 mos. | Green (cloudy) | ..... | ... | 5.2181 | Partly filled pint bottle |
| 10–28–27 | 11 mos. | Green (cloudy) | ..... | ... | 5.1793 | Partly filled pint bottle |
| 11–28–27 | 1 year | Green (cloudy) | ..... | ... | 5.1793 | Partly filled pint bottle |
| 1–15–28 | 14 mos. | Green (cloudy) | ..... | ... | 5.1019 | Partly filled pint bottle |
| 3–19–28 | 16 mos. | Green (cloudy) | ..... | ... | 5.2640 | Partly filled pint bottle |
| 7–16–28 | 20 mos. | Brown | ..... | ... | 5.218 | Partly filled pint bottle |

TABLE VIII.

SAMPLE A. KEPT IN SMALL COMPLETELY FILLED, TIGHTLY CORKED ONE-OUNCE BOTTLES; EACH OPENED ONLY AT THE TIME OF THE SPECIFIC ASSAY.

| Date. | Age. | Color. | Scum. | Free iodine. | % $FeI_2$. | Remarks. |
|---|---|---|---|---|---|---|
| 10–26–26 | .... | Green | ... | ... | 5.2531 | .... |
| 11–27–26 | 1 mo. | Green | ... | ... | 5.2181 | .... |
| 12–28–26 | 2 mos. | Green | ... | ... | 5.178 | .... |
| 2– 1–27 | 3 mos. | Green | ... | ... | 5.2181 | .... |
| 3– 3–27 | 4 mos. | Green | ... | ... | 5.2181 | .... |
| 4– 9–27 | 5 mos. | Green | ... | ... | 5.1793 | .... |
| 5–23–27 | 6 mos. | Green | ... | ... | 5.1793 | .... |
| 6–25–27 | 7 mos. | Green | ... | ... | 5.1793 | .... |
| 9–20–27 | 10 mos. | Green | ... | ... | 5.2181 | .... |
| 10–28–27 | 11 mos. | Green | ... | ... | 5.1406 | .... |
| 11–28–27 | 1 year | Green | ... | ... | 5.1019 | .... |
| 1–15–28 | 14 mos. | Green | ... | ... | 5.1793 | .... |
| 3–19–28 | 16 mos. | Green | ... | ... | 5.2645 | .... |
| 7–16–28 | 20 mos. | Brownish green | ... | ... | 5.1793 | .... |

These three samples were stored as in the case of those used in Part I; that is (*a*) a filled pint bottle; (*b*) a partly filled pint bottle; (*c*) the rest in completely filled well-stoppered one-ounce bottles which were opened only as they were as-

[1] The invert sugar used was the "Nulomoline" brand, the amount used corresponding to 850 Gm. of 100% material to 1000 cc. of finished syrup.

sayed. Samples A and B were prepared October 20, 1926, and Sample C two days later. As in Part I the color, presence of scum, presence of free iodine and the iodide assay was carefully studied with results noted in the tables:

TABLE IX.

SAMPLE B. SUCCESSIVE ASSAYS OF SAME SAMPLE STORED IN 2 ONE-PINT BOTTLES. UNDER "REMARKS," MENTION IS MADE AS TO WHETHER THE ASSAYED SAMPLE WAS TAKEN FROM THE FULL OR PARTLY FULL BOTTLE.

| Date. | Age. | Color. | Scum. | Free iodine. | % $FeI_2$. | Remarks. |
|---|---|---|---|---|---|---|
| 10–26–26 | .... | Green | ... | ... | 5.4116 | Partly filled pint bottle |
| 11–27–26 | 1 mo. | Green | ... | ... | 5.3419 | Full pint bottle |
| 12–28–26 | 2 mos. | Green | ... | ... | 5.403 | Full pint bottle |
| 2– 1–27 | 3 mos. | Green | ... | ... | 5.4115 | Full pint bottle |
| 3– 3–27 | 4 mos. | Green | ... | ... | 5.45036 | Full pint bottle |
| 4– 9–27 | 5 mos. | Green | ... | ... | 5.45036 | Full pint bottle |
| 5–23–27 | 6 mos. | Dull green | ... | ... | 5.45036 | Full pint bottle |
| 6–25–27 | 7 mos. | Dull green | ... | ... | 5.45036 | Full pint bottle |
| 9–20–27 | 10 mos. | Dull green | ... | ... | 5.4503 | Partly filled pint bottle |
| 10–28–27 | 11 mos. | Dull green | ... | ... | 5.4503 | Partly filled pint bottle |
| 11–28–27 | 1 year | Dull green | ... | ... | 5.5277 | Partly filled pint bottle |
| 1–15–28 | 14 mos. | Dull green | ... | ... | 5.4890 | Partly filled pint bottle |
| 3–19–28 | 16 mos. | Dull green | ... | ... | 5.4968 | Partly filled pint bottle |
| 7–16–28 | 20 mos. | Dull green | ... | ... | 5.4890 | Partly filled pint bottle |

TABLE X.

SAMPLE B. KEPT IN SMALL, COMPLETELY FILLED, TIGHTLY CORKED ONE-OUNCE BOTTLES; EACH OPENED ONLY AT THE TIME OF THE SPECIFIC ASSAY.

| Date. | Age. | Color. | Scum. | Free iodine. | % $FeI_2$. | Remarks. |
|---|---|---|---|---|---|---|
| 10–26–26 | .... | Green | .... | .... | 5.4116 | .... |
| 11–27–26 | 1 mo. | Green | .... | .... | 5.4116 | .... |
| 12–28–26 | 2 mos. | Green | .... | .... | 5.334 | .... |
| 2– 1–27 | 3 mos. | Green | .... | .... | 5.4503 | .... |
| 3– 3–27 | 4 mos. | Green | .... | .... | 5.4503 | .... |
| 4– 9–27 | 5 mos. | Green | .... | .... | 5.3729 | .... |
| 5–23–27 | 6 mos. | Green | .... | .... | 5.3679 | .... |
| 6–25–27 | 7 mos. | Green | .... | .... | 5.4503 | .... |
| 9–20–27 | 10 mos. | Green | .... | .... | 5.4890 | .... |
| 10–28–27 | 11 mos. | Green | .... | .... | 5.4116 | .... |
| 11–28–27 | 1 year | Green | .... | .... | 5.3729 | .... |
| 1–15–28 | 14 mos. | Green | .... | .... | 5.4116 | .... |
| 3–19–28 | 16 mos. | Green | .... | .... | 5.4194 | .... |
| 7–16–28 | 20 mos. | Green | .... | .... | 5.4194 | .... |

TABLE XI.

SAMPLE C. SUCCESSIVE ASSAYS OF THE SAME SAMPLE STORED IN 2 ONE-PINT BOTTLES. UNDER "REMARKS," MENTION IS MADE WHETHER THE ASSAYED SAMPLE WAS TAKEN FROM THE FULL OR PARTLY FULL BOTTLE.

| Date. | Age. | Color. | Scum. | Free iodine. | % $FeI_2$. | Remarks. |
|---|---|---|---|---|---|---|
| 10–26–26 | .... | Bright green | .... | .... | 5.0942 | Partly filled pint bottle |
| 11–27–26 | 1 mo. | Bright green | .... | .... | 5.0942 | Full pint bottle |
| 12–28–26 | 2 mos. | Bright green | .... | .... | 4.978 | Full pint bottle |
| 2– 1–27 | 3 mos. | Bright green | .... | .... | 5.0555 | Full pint bottle |
| 3– 3–27 | 4 mos. | Bright green | .... | .... | 5.0555 | Full pint bottle |
| 4– 9–27 | 5 mos. | Bright green | .... | .... | 5.0942 | Full pint bottle |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5–23–27 | 6 mos. | Bright green | .... | .... | 5.0555 | Full pint bottle |
| 6–25–27 | 7 mos. | Bright green | .... | .... | 5.0942 | Full pint bottle |
| 9–20–27 | 10 mos. | Bright green | .... | .... | 5.0168 | Partly filled pint bottle |
| 10–28–27 | 11 mos. | Bright green | .... | .... | 5.0168 | Partly filled pint bottle |
| 11–28–27 | 1 year | Bright green | .... | .... | 5.0477 | Partly filled pint bottle |
| 1–15–28 | 14 mos. | Bright green | .... | .... | 5.0942 | Partly filled pint bottle |
| 3–19–28 | 16 mos. | Bright green | .... | .... | 5.1984 | Partly filled pint bottle |
| 7–20–28 | 20 mos. | Bright green | .... | .... | 5.0168 | Partly filled pint bottle |

TABLE XII.

SAMPLE C. KEPT IN SMALL, COMPLETELY FILLED, TIGHTLY CORKED ONE-OUNCE BOTTLES; EACH OPENED ONLY AT THE TIME OF THE SPECIFIC ASSAY.

| Date. | Age. | Color. | Scum. | Free iodine. | % FeI₂ | Remarks. |
|---|---|---|---|---|---|---|
| 10–26–26 | .... | Bright green | .... | .... | 5.0942 | .... |
| 11–27–26 | 1 mo. | Bright green | .... | .... | 5.0942 | .... |
| 10–28–26 | 2 mos. | Bright green | .... | .... | 5.016 | .... |
| 2– 1–27 | 3 mos. | Bright green | .... | .... | 5.0555 | .... |
| 3– 3–27 | 4 mos. | Bright green | .... | .... | 5.0555 | .... |
| 4– 9–27 | 5 mos. | Bright green | .... | .... | 5.0166 | .... |
| 5–23–27 | 6 mos. | Bright green | .... | .... | 5.0555 | .... |
| 6–25–27 | 7 mos. | Bright green | .... | .... | 5.0492 | .... |
| 9–20–27 | 10 mos. | Bright green | .... | .... | 5.0555 | .... |
| 10–28–27 | 11 mos. | Bright green | .... | .... | 5.0169 | .... |
| 11–28–27 | 1 year | Bright green | .... | .... | 5.1019 | .... |
| 1–15–28 | 14 mos. | Bright green | .... | .... | 5.1019 | .... |
| 3–19–28 | 16 mos. | Bright green | .... | .... | 5.1484 | .... |
| 7–16–28 | 20 mos. | Bright green | .... | .... | 5.0942 | .... |

The following comments on the three Samples A to C, supplement the tables just given:

The 1926–1928 samples kept much better than the samples of 1924–1926. This is possibly due to the use of absolutely new bottles, just as they came from the factory. Perhaps these fresh containers were in a more sterile condition than the old but well-cleaned bottles used in the first set of experiments.

The puzzling behavior as to question of presence or absence of free iodine shown in Tables I and II (the real cause of repeating the work), may be due to the fact that the 1924 experiments were carried on in a room where artificial light was necessary most of the time whereas the 1926–1928 experiments were conducted in a room receiving an abundance of sunshine.

The "scum" noted in the 1924 experiments was noted only in Sample A of 1926–1928 and in a lesser amount; possibly due to the influence of sunlight; in fact, the amount available was too small to repeat the chemical examinations of 1924.

The darkening of the silver iodide precipitate during the assay of Sample A was as noticeable as it was in the 1924 experiments. No mention is made of it, however, in the tables.

Sample C kept more satisfactorily than the other two, suggesting the possible value of invert sugar as a sweetener and preservative of this official syrup.

## *Part III.*—THE HYDRIODIC PREPARATIONS.

(Work performed with Benjamin Vener, Ph.G., B.S.)

While our main object was to study the stability of syrup of hydriodic acid,

since this pharmaceutical is made from the diluted acid, the latter product had to be given consideration. Only one sample of the diluted acid was prepared, since that sample proved entirely satisfactory. From this sample (which we will call Sample E) three samples of the syrup were prepared; Sample F made with an old sample of simple syrup giving a positive reaction for reducing sugar; Sample G made with a freshly prepared simple syrup giving a negative reaction for reducing sugar; and Sample H made by diluting 125 cc. of the diluted acid with a mixture of 375 Gm. syrup and 400 Gm. glycerin followed by enough water to make the finished product measure 1000 cc. Samples E and F were assayed over a period of 20 weeks under conditions described in the discussion of the samples of syrup of ferrous iodide A and B. Syrup of hydriodic acid, Sample G, was assayed when fresh and when 16 weeks and when 21 months old, while Sample H was assayed when fresh and when 12 weeks and 19 months old. Incidentally it might be stated that the main objects in preparing the three samples of the syrup were (*a*) to study the effect of an old simple syrup (containing reducing sugars) on the stability and the titration of the preparation; (*b*) to find if the presence of glycerin would improve the product.

The following are the tabulated results of our experiments with the hydriodic preparations:

TABLE XIII.

SAMPLE E (DILUTED HYDRIODIC ACID). SUCCESSIVE ASSAYS OF SAME SAMPLE CONTAINED IN AN INCOMPLETELY FILLED BOTTLE.

| Age. | Color. | Titration. % HI. | AgI ppt. |
|---|---|---|---|
| Fresh | Colorless | 9.645 | Reduced |
| 1 week | Colorless | 9.78 | Reduced |
| 2 weeks | Colorless | 9.78 | Reduced |
| 3 weeks | Colorless | 9.78 | Reduced |
| 4 weeks | Colorless | 9.78 | Reduced |
| 8 weeks | Colorless | 9.633 | Reduced |
| 12 weeks | Colorless | 9.633 | Reduced |
| 16 weeks | Colorless | 9.751 | Reduced |
| 20 weeks | Colorless | 9.751 | Reduced |
| 22 months | Colorless | 9.841 | Reduced |

TABLE XIV.

SAMPLE E (DILUTED HYDRIODIC ACID). KEPT IN SMALL, COMPLETELY FILLED, TIGHTLY CORKED BOTTLES EACH OPENED ONLY AT THE TIME OF THE SPECIFIC ASSAY.

| Age. | Color. | Titration. % HI. | AgI ppt. |
|---|---|---|---|
| Fresh | Colorless | 9.645 | Reduced |
| 1 week | Colorless | 9.78 | Reduced |
| 2 weeks | Colorless | 9.78 | Reduced |
| 3 weeks | Colorless | 9.78 | Reduced |
| 4 weeks | Colorless | 9.71 | Reduced |
| 8 weeks | Colorless | 9.633 | Reduced |
| 12 weeks | Colorless | 9.633 | Reduced |
| 16 weeks | Colorless | 9.751 | Reduced |
| 20 weeks | Colorless | 9.751 | Reduced |

TABLE XV.

SAMPLE F (SYRUP OF HYDRIODIC ACID). SUCCESSIVE ASSAYS OF SAME SAMPLE CONTAINED IN AN INCOMPLETELY FILLED BOTTLE.

| Age. | Color. | Titration. Gm. HI in 100 cc. | AgI ppt. |
|---|---|---|---|
| Fresh | Colorless | 1.201 | Reduced |
| 1 week | Colorless | 1.213 | Reduced |
| 2 weeks | Colorless | 1.201 | Reduced |
| 3 weeks | Colorless | 1.201 | Reduced |
| 4 weeks | Colorless | 1.201 | Reduced |
| 8 weeks | Colorless | 1.185 | Reduced |
| 12 weeks | Colorless | 1.185 | Reduced |
| 16 weeks | Colorless | 1.235 | Reduced |
| 20 weeks | Colorless | 1.235 | Reduced |
| 22 months | Faint straw | 1.379 | No reduction |

TABLE XVI.

SAMPLE F (SYRUP OF HYDRIODIC ACID). KEPT IN SMALL, COMPLETELY FILLED, TIGHTLY CORKED BOTTLES, EACH OPENED ONLY AT THE TIME OF THE SPECIFIC ASSAY.

| Age. | Color. | Titration. Gm. HI in 100 cc. | AgI ppt. |
|---|---|---|---|
| Fresh | Colorless | 1.201 | Reduced |
| 1 week | Colorless | 1.213 | Reduced |
| 2 weeks | Colorless | 1.227 | Reduced |
| 3 weeks | Colorless | 1.227 | Reduced |
| 4 weeks | Colorless | 1.227 | Reduced |
| 8 weeks | Colorless | 1.173 | Reduced |
| 12 weeks | Colorless | 1.173 | Reduced |
| 16 weeks | Colorless | 1.259 | Reduced |
| 20 weeks | Colorless | 1.259 | Reduced |

TABLE XVII.

SAMPLE G (SYRUP OF HYDRIODIC ACID). THREE ASSAYS OF SAME SAMPLE CONTAINED IN AN INCOMPLETELY FILLED BOTTLE.

| Age. | Color. | Titration. Gm. HI in 100 cc. | AgI ppt. |
|---|---|---|---|
| Fresh | Colorless | 1.319 | No reduction |
| 16 weeks | Colorless | 1.367 | No reduction |
| 21 months | Faint straw | 1.355 | Reduction |

TABLE XVIII.

SAMPLE H (SYRUP OF HYDRIODIC ACID). FOUR ASSAYS OF THE SAME SAMPLE CONTAINED IN AN INCOMPLETELY FILLED BOTTLE.

| Age. | Color. | Titration. Gm. HI in 100 cc. | AgI ppt. |
|---|---|---|---|
| Fresh | Colorless | 1.395 | No reduction |
| 1 week | Colorless | 1.395 | No reduction |
| 12 weeks | Colorless | 1.450 | No reduction |
| 19 months | Faint straw | 1.438 | Faint reduction |

Commenting on Tables XIII to XVIII, it must be stated that the sample of diluted hydriodic acid and the three samples of syrup of hydriodic acid kept perfectly, there being during the 20 weeks no indication of darkening, of the presence of iodine, or the production of a sediment. In short, the stability of the U. S. P. diluted acid and the syrup is so satisfactory that there is no need of amending the

official recipe even to the extent of using glycerin as a preservative. In connection with the use of glycerin, it has been stated (9) that the addition of glycerin causes hydriodic preparations to develop a bad odor ("horrible odor," one observer states). Our samples containing glycerin that are almost two years old have nothing more than a slightly sour smell. The titration of the hydriodic preparations are not easy since the precipitated silver iodide not only darkens but frequently assumes a blue-purple tint that causes difficulty in determining the end-point of the titration.

In short there are a number of factors interfering with the sensitivity of the titration of syrup of hydriodic acid as directed by the U. S. P. "Blank titrations" of solutions containing sugar and potassium hypophosphite showed little or no reduction either visually or when expressed in terms of tenth-normal silver nitrate and thiocyanate, respectively. A solution containing sugar and diluted hypophosphorous acid, however, quickly reduced the silver solution. Old syrup diluted with water containing potassium hypophosphite had no more effect upon the silver solution than had a fresh syrup. So apparently the reduction of the silver salt in the titration of these preparations occurs primarily in the presence of silver iodide. The subject is one worthy of more study but is one which is hardly within the scope of this paper, hence we will close by merely stating that we obtained more satisfactory titration results by diluting the sample of the syrup (either ferrous iodide or hydriodic acid) with *warm* water and then adding the ferric alum solution followed by the nitric acid prior to titration with the thiocyanate solution. This, we found, usually obviates the warming on a water-bath in the presence of nitric acid, directed by the Pharmacopœia, as a means to reconverting the reduced silver precipitate to the yellow silver iodide.

## *Part IV.*—CONCLUSIONS.

1. The U. S. P. recipe for syrup of hydriodic acid is satisfactory, the resulting product being quite stable.
2. The U. S. P. recipe for syrup of ferrous iodide is less satisfactory, since the resulting product turns yellow and shows traces of precipitation.
3. In such deterioration, the decrease in iodide content is negligible and the amount of iodine liberated is insignificant.
4. The turbidity (or "scum") found in samples of the official syrup of ferrous iodide appears to be ferric hypophosphite. The formation of this "scum" is less noticeable in samples exposed to sunlight than in those kept in a dark place.
5. The syrup when free from a stabilizer does liberate iodine and the freed iodine may be returned into chemical combination by action of direct sunlight.
6. The U. S. P. syrup (containing hypophosphorous acid) suffered more decomposition on standing than the other samples.
7. The omission of hypophosphorous acid and the use of glycerin as a stabilizer does not yield a satisfactory product.
8. A sample of Syrup of Ferrous Iodide made with invert sugar was found practically perfect after standing 22 months.

## *Part V.*—BIBLIOGRAPHY.

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COLUMBIA UNIVERSITY,
COLLEGE OF PHARMACY,
July 1928.

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# A PHARMACEUTICAL STUDY OF MAGMÆ MAGNESIÆ—1900–1930.

BY A. J. LEHMAN, M.S.

(*Continued from p. 265, March Issue*).

## 5. SODIUM HYDROXIDE AS AN INGREDIENT.

Sodium hydroxide is prescribed by all three standards containing Magma Magnesia. The 1900 N. F. prescribed 81 Gm., the U. S. P. of 1910, 80 Gm. and the U. S. P. revision of 1920 increased the amount to 100 Gm., each for 1000 cc. of product. The purity rubric for the last three revisions reads "not less than 90 per cent of NaOH." Based upon this 81 Gm., 80 Gm. and 100 Gm. of sodium hydroxide represent 72.9 Gm., 72 Gm. and 90 Gm. of NaOH. Other alkalies were suggested in place of sodium hydroxide. An unsigned article (29) (1896) includes a formula for a "Fluid magnesia" in which sodium carbonate is prescribed. A second formula (30) (1904) prescribes "solution of potash—enough."

Raubenheimer (31) (1907) in commenting on this ingredient prefers NaOH to KOH in preparing milk of magnesia because of the greater solubility of the formed sodium sulphate which makes it easier to wash out. Terry and Davy (32) (1920) are also in favor of sodium hydroxide because of the cost. Ammonia should not be used they claim as magnesium hydroxide is soluble in ammonia. Grosh (33) (1913) contrary to this statement says that using stronger ammonia water, gives a more rapid precipitation and also eliminates filtering.

In respect to the quantity of sodium hydroxide used Bruden (34) (1909) suggests increasing the sodium hydroxide by one-half while Diehl (35) (1909) suggests a reduction to 72 Gm. Cloughy (36) (1913) increases the quantity to 81 Gm., Hilton (37) (1911) to 119 Gm. and Beringer (38) (1913) to 100 Gm. McNeery (39) (1916) for one gallon of magma uses 6259.08 grains or about 405 Gm., representing about 101 Gm. per 1000 cc. Mueller (40) (1917) offers an increase to 120 Gm., Boehm (41) (1908) to 125 Gm.

The following table summarizes the quantities of sodium hydroxide directed to be used by the official as well as by non-official formulas together with the respective absolute equivalents.

| Formula. | Sodium hydroxide. | Purity rubric. | Absolute. |
|---|---|---|---|
| N. F. 1900 | 81 | 90% | 72.9 Gm. NaOH |
| U. S. P. 1910 | 80 | 90 | 72.0 Gm. NaOH |
| U. S. P. 1920 | 100 | 90 | 90 Gm. NaOH |

| Formula. | Sodium hydroxide. | Purity rubric. | Absolute. |
|---|---|---|---|
| Raubenheimer | 81 | 90 | 72.9 Gm. NaOH |
| Boehm | 125 | 90 | 112.5 Gm. NaOH |
| Posey | 81 | 90 | 72.9 Gm. NaOH |
| Bruden | 121.5 | 90 | 112.95 Gm. NaOH |
| Diehl | 72 | 90 | 64.8 Gm. NaOH |
| Hilton | 119 | 90 | 107.1 Gm. NaOH |
| Beringer | 100 | 90 | 90 Gm. NaOH |
| Mueller | 120 | 90 | 108 Gm. NaOH |

### 6. RATIO OF INGREDIENTS.

The following equation may be used to represent the reaction taking place when the Magma is prepared according to the National Formulary process.

(*1*) $MgSO_4$ + 2NaOH + $Mg(OH)_2$ + $Na_2SO_4$
120.39 80.02
1 0.664
121.475 79.9

Inasmuch as only 72.9 Gm. of NaOH are prescribed, the theoretical deficiency is 7.0 Gm.

(*2*) 2NaOH + $MgSO_4$ = $Mg(OH)_2$ + $Na_2SO_4$
80.02 120.39
1 1.504
72.9 109.641

Inasmuch as 121.475 Gm. of $MgSO_4$ are prescribed, the excess present is 10.83 Gm.

The equation representing the reaction taking place when the Magma is prepared according to the U. S. P. 1900 method may be represented by the following:

(*1*) MgO + 2NaOH = $Mg(OH)_2$ + $Na_2O$ (Theory)
40.32 80.02
1 1.94
49 97.216

Inasmuch as only 72 Gm. of NaOH are prescribed the theoretical defficiency is 25.216 Gm.

(*2*) 2NaOH + MgO = $Mg(OH)_2$ + $Na_2O$ (Theory)
80.02 40.32
1 0.503
72 36.216

Inasmuch as the equivalent of 49 Gm. of MgO is prescribed the equivalent MgO in excess is 12.784 Gm.

The U. S. P. revision of 1920 reverted to the use of magnesium sulphate. Based upon the equations given above:

145.8 Gm. of $MgSO_4$ require 96.81 Gm. of NaOH.
160.45 Gm. of $MgSO_4$ require 106.54 Gm. of NaOH.
90 Gm. of NaOH require 135.36 Gm. of $MgSO_4$

Hence there is prescribed an excess of 10.44 Gm. to 25.09 Gm. of $MgSO_4$ or a deficiency of 6.81 Gm. to 16.54 Gm. of NaOH occurs.

From the above the following becomes apparent, *viz.:* (*a*) That according to the N. F. process the amount of Magnesium Hydroxide in the finished product is that represented by 109.641 Gm. of $MgSO_4$. (*b*) That according to the U. S. P. 1910 process the amount of Magnesium Hydroxide in the finished product, that resulted from the interaction between the salt and the alkali is that represented by 72 Gm. of NaOH. (*c*) That according to the U. S. P. 1920 process the amount of Magnesium Hydroxide present in the finished product is that represented by 135.36 Gm. of $MgSO_4$.

Based upon this the following becomes apparent:

| | | | |
|---|---|---|---|
| (*a*) | $MgSO_4$ | = | $Mg(OH)_2$ |
| | 120.39 | | 58.04 |
| | 1 | | 0.484 |
| | 109.6 | | 53.065 Gm. of $Mg(OH)_2$ in 1000 cc. of product. |
| (*b*) | 2NaOH | = | $Mg(OH)_2$ |
| | 80.02 | | 58.34 |
| | 1 | | 0.729 |
| | 72 | | 52.788 Gm. of $Mg(OH)_2$ in 1000 cc. of product. |
| (*c*) | $MgSO_4$ | = | $Mg(OH)_2$ |
| | 120.39 | | 58.34 |
| | 1 | | 0.484 |
| | 105.36 | | 65.514 Gm. of $Mg(OH)_2$ in 1000 cc. of product. |

SUMMARY TABLE.

| Formula. | NaOH. | $MgSO_4$. | $MgSO_4$ required. | Excess. | $Mg(OH)_2$ in 1000 cc. |
|---|---|---|---|---|---|
| N. F. IV | 72.9 | 121.475 | 109.641 | 10.80 | 53.06 Gm. |
| U. S. P. 1910 | 90.0 | 14.58 | 135.36 | 10.44 | 65.51 Gm. |
| | | 160.45 | | 25.09 | |
| Raubenheimer | 72.9 | 166.16 | 109.641 | 56.519 | 53.06 Gm. |
| Boehm | 112.5 | 121.475 | 168.75 | ..... | 53.06 (NaOH in excess) |
| Bruder | 112.95 | 121.475 | 169.50 | ..... | 53.06 (NaOH in excess) |
| Diehl | 64.8 | 106.898 | 97.20 | 9.698 | 47.05 Gm. |
| Hilton | 107.10 | 170.065 | 160.63 | 9.435 | 70.74 Gm. |
| Beringer | 90.0 | 121.475 | 135.36 | ..... | 53.06 (NaOH in excess) |
| Mueller | 108.0 | 268.65 | 162.4 | 106.25 | 51.42 Gm. |
| Posey | 72.9 | 108.84 | 109.641 | ..... | 52.67 Gm. |

## 7. WATER.

The N. F. 1900 does not specify that distilled water be used in the preparation of the magma. It does, however, state in a note that "the water used in preparing this must be free from organic matter or the magma will become discolored."

The U. S. P. 1910 prescribes that distilled water be used throughout the entire process. It also includes a note which states, "the distilled water in this preparation may be replaced by water which has been heated to boiling with powdered Magnesium Carbonate, 5 Gm., in 1000 mils and then filtered." The revision of 1920 prescribes distilled water.

Distilled water is somewhat expensive for the average pharmacist to use and various suggestions have been made to overcome this obstacle. Raubenheimer (42) (1907) says water used in preparing the magma must be free from organic matter. He suggests using Scoville's (43) (1903) method of purifying it, that of adding 2 grains of alum to each gallon of water to precipitate the organic matter. Cliffe (44)

(1910) experimented with filtered river water but found the magma became discolored. Beringer (45) (1913) states that if distilled water cannot be obtained, water which has been boiled with magnesium carbonate 5 Gm. to 1000 cc. will prove satisfactory. Needham (46) (1910) mentions using hot water previously boiled to free from organic matter.

8. METHOD OF PREPARATION.

*A. Solution or Suspension of the Magnesium Salt.*—The N. F. 1900 formula calls for 4000 cc. (or 128 ounces) of water to dissolve the magnesium sulphate. The U. S. P revision of 1910 directs that the magnesium carbonate be mixed with sufficient distilled water to make a smooth mixture, about 500 cc. being sufficient and the revision of 1920 prescribes distilled water to make 650 cc. The concentration of this solution has brought about numerous comments. Bruder (47) (1909) reduces the volume to 500 cc. in order to obtain a heavier precipitate when the two solutions are mixed; Hilton (48) (1911) follows this closely by dissolving the salt in 400 cc. of distilled water. Beringer (49) (1913) prescribes 1000 cc., while Mueller (50) (1917) directs using 700 cc. of water.

*B. Solution of Sodium Hydroxide.*—The N. F., 1900, prescribes 4000 cc. (or 128 ounces) of water for the solution of the sodium hydroxide. The U. S. P. revision of 1910 called for 400 mils of distilled water while the revision of 1920 prescribes sufficient distilled water to make 1000 cc. In commenting on the N. F. formula Bruder (51) (1909) reduces the volume to 500 cc. Hilton (52) (1911) prescribes 700 cc.; Beringer (53) (1913) 1000 cc. and Mueller (54) (1910) only 250 cc. Other concentrations are offered for both solutions of magnesium sulphate and sodium hydroxide, but all practically come within the two extremes reported here.

*C. Order of Mixing the Solutions.*—According to the N. F. 1900 the two solutions are filtered separately and then the Sodium Hydroxide solution poured "slowly and in a thin stream into the Magnesium Sulphate solution with constant stirring." According to the U. S. P. 1910 the sodium hydroxide solution is added to the Magnesium Carbonate mixture, with constant stirring and frequent agitation during 15 minutes, and the revision of 1920 again directs the addition "slowly" of the sodium hydroxide to the magnesium sulphate solution. Caldwell (55) (1906) favors a reversal of the order, claiming a better magma, whereas Dunn (56) (1911) emphasizes the pouring of the alkali solution into the magnesium sulphate solution "in a fine stream and with constant stirring." Beringer (57) (1913) supports Dunn claiming an advantage of an excess of alkali during the precipitation. Others supporting this order of mixing are Hensel (58) (1914) and Mills (59) (1914).

*D. Hot or Cold Solutions.*—No mention of the use of heat is made in the formulas of 1900 and 1910. The U. S. P. revision of 1920 directed that the magnesium sulphate solution be boiling and that the boiling be continued for thirty minutes after the addition of the sodium hydroxide solution. Caldwell (60) (1906) directed the use of hot solutions. Beringer (61) (1913) also favors hot solutions and Cloughy (62) (1913) prescribes a temperature of 70° C. Possehl (63) (1914) directs heating the solutions after mixing, slowly stirring and boiling for 15 minutes. Hensel (64) (1914), Mills (65) (1914) and Hilton (66) (1911) all favor hot solutions.

*E. Washing the Magma.*—The N. F. 1900 directs that the magma should be washed by decantation until the washings are free from saline taste. The U. S. P.

1910 states: "Wash the resulting magma by decantation using two thousand mils of water each time until the red color produced in 50 mils of the washings by 3 drops of phenolphthalein T. S. is discharged by one drop of diluted sulphuric acid," while the U. S. P. 1920 simply directs the use of sufficient hot distilled water, washing repeatedly until the washings show no sulphates with barium chloride T. S. Apparently most of the comments deal with the technique of washing rather than the volumes of wash water used. Raubenheimer (67) (1907) suggests removing the water by syphoning; Boehm (68) (1908) suspends the magma in an inverted percolater and washes by percolation. This procedure is approved of by Diehl (69) (1909) and Beringer (70) (1910). Hilton (71) (1911) dilutes the magma to 3000 cc. and allows it to settle to the 1000 mark, syphons off the supernatant liquid, again adding 2500 cc. of water, repeating this twice followed by the addition of 4000 cc. for the final washing. Hensel (72) (1914) washes with five times as much distilled water, as the volume of finished product, doing this about five times. McNeery (73) (1916) directs washing the precipitate by either decantation or siphoning until the washings are neutral to litmus. Hensel (74) (1915) finds four washings sufficient and Terry (75) (1919) washes the hot magma by boiling with twice as much water as product desired, and repeating twice.

*F. Collecting the Magma.*—According to the N. F. 1900 the magma is collected on a muslin strainer, allowed to drain without pressing, then transferred to suitable vessels and sufficient water added to make 1000 cc. The U. S. P. 1910 directs that the magma be allowed to subside till it measures 1000 cc. and the supernatant liquid decanted, while the revision of 1920 prescribes concentration "by evaporation" to required volume.

Raubenheimer (76) (1907) states that the precipitate should not be drained because of danger of $CO_2$ absorption. Sennewald (77) (1907) reports difficulty in obtaining a precipitate that could be collected on a strainer. Furthermore that the "settling" takes place so slowly. Boehm (78) (1908) suggests placing the magma in a percolator, then fastening a layer of cheese cloth over the mouth, inverting, washing and collecting the magma in this manner. Hilton (79) (1911) directs that the washed magma be allowed to subside to the required volume. Beringer (80) (1913) calls for a muslin strainer for collecting the precipitate while Hensel (81) (1915) favors a filter paper and the removal of the precipitate with a silver spoon. Sayre (82) (1917) reports that three weeks would be required to wash and collect the precipitate according to the U. S. P. directions. That the final subsidation required nearly a week alone; the use of a centrifuge facilitates the collection of the magma.

The U. S. P. 1920 directs "concentrate the mixture by evaporation until it contains not less than 7 per cent of magnesium hydroxide" may not be a solution of the difficulty. No temperature is mentioned and as one may assume from the differences of opinion as to the use of heat in making the magma, the application of varying temperatures for evaporation may influence the nature of the final product.

*(To be concluded)*

# DEPARTMENT OF BUSINESS MANAGEMENT

Conducted by Paul C. Olsen.*

## COMMENTS, QUESTIONS AND SUGGESTIONS ARE INVITED AND WELCOME.

Readers are invited to submit comments, criticisms and suggestions regarding the material which appears in this department. The Editor also will undertake to answer questions regarding general problems of business management. Letters of general interest will be published, but the writer's name will not be revealed without his permission.

## HOW MUCH PRESCRIPTION BUSINESS IS THERE?

(*Continued from p. 283, March Issue*)

Horace Hampton, progressive Centertown druggist, and his friend and classmate, Lloyd Hamel, of Cleartown, were enjoying the 17-cent cigars which Mr. Hampton had abstracted from the case before they had gone to lunch.

"This has been very pleasant," began Mr. Hamel, "I've enjoyed seeing you and it's been a pleasure for me to get your ideas on how profitable a good volume of prescriptions can be. But, Horace, as you said just before we went out, there is a big difference between knowing that a worth-while number of prescriptions would be profitable and actually getting those prescriptions."

"Just a minute—not so fast, Lloyd," interrupted Hampton. "You've left out an in-between step which is just as important.

"You could put your store in the middle of the Sahara desert and work hard from now until you're ninety and you wouldn't do any business in prescriptions or anything else. For all you and I know, Cleartown may be a Sahara desert as far as prescriptions go and you'd only be wasting valuable time and good money in an effort to get something which wasn't to be had.

"How many practicing physicians are there in Cleartown?"

"Oh, twenty or twenty-one, I'd say, Horace."

"Now of course it would be fine to know how many prescriptions each doctor writes a day, but of course it's next to impossible to find out—at least not directly."

"I see what you're driving at, Horace; the total number of prescriptions written daily in Cleartown is the total amount of such business to be had. If that is a worth-while amount and my five competitors aren't too strongly entrenched, it's up to me to get my share or more than my share of this total volume. But how in the world can anybody find out even indirectly how many prescriptions our physicians write?"

"It isn't as difficult as you might think at first, Lloyd. Start this way. It's just a case of resolving the thing into its component parts. I'll bet you know every one of the physicians in Cleartown by name—probably a lot of them by their first names. If you don't, you should.

"Write the names of each one of these physicians on a sheet of paper and after each man's name write the number of prescriptions you think that man averages a day.

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"If you have any doubt about any particular name, go to him frankly and tell him that you are trying to get an idea of the volume of prescriptions that are being written in Cleartown.

"You know and I know that physicians time and time again have given far more confidential information to responsible people, so you should feel no hesitancy in asking this from those men the extent of whose prescription writing you can't estimate yourself.

"From your own knowledge and from what physicians will tell you, you thus obtain at least a careful estimate of the total amount of prescription business that is available in Cleartown. Notice that this estimate is apt to be high, for psychological reasons, but none the less it gives a fair idea of the amount of this business there is to be had.

"Then divide that estimate by the six drug stores in Cleartown and you have an idea of what your share ought to be. Of course, you hope eventually to get more than your share, but if you're only filling one or two prescriptions a day, I'm dead sure, without looking any further, that you're not getting your share.

"You understand, of course, that this total volume of prescriptions will vary from month to month; you've been in the drug-store business too long for me to have to tell you which are the best prescription months.

"One more thing about the prescription business, and it's a thing often overlooked by druggists who are wondering how they can increase their sales and profits in prescriptions. Curiously enough, a big share of the profits of a prescription department can come from sales which aren't prescriptions at all. I mean olive oil, castor oil, syrup of ipecac and a thousand related items. It's useless for me to try to list them from memory because I might omit some of the most important ones, and mention others for which you would have no demand. The simplest way to do is to start with the A's in the prescription room stock and go right down the line checking off preparations that you consider salable. It's amazing how many of the simplest remedies are missing from the average home medicine chest. Look around in your friends' homes and be convinced.

"Remember, though, that you can't carry water on both shoulders. You can't expect physicians to coöperate with you if you plaster your store with suggestions about self-medication. On the other hand, physicians actually encourage druggists to push the old, time-tried preparations that everybody knows about.

"This applies not only to the items which are primarily medicines, but also to such things as flavoring extracts and spices. Druggists will tell you that the bulk of that business has gone to grocery stores and that it's pretty nearly hopeless for a druggist to try to get much of it from them. The grocers got it through the medium of low prices and that's the way they're keeping it. There are still great numbers of people who appreciate quality and the druggist's big opportunity is to get a share of the business on that basis.

"Of course, I'm only speculating. It's up to you to find out if you can sell a worth-while amount of these classes of prescription-room merchandise. You have learned that proper display will sell candy and toilet articles and a lot of other things that formerly were not featured in drug-store lines. At small expense and trouble you can find out about the sales possibilities of these other goods."

"But that doesn't tell me how to get people to bring their prescriptions to my store, Horace," protested Mr. Hamel.

"No, indeed, it doesn't. Come back to the store and I'll show you some of the things I had to do to get my share of the prescription business. I've only been trying to explain how to determine whether or not you have in Cleartown enough prescription business worth going after."

*(To be concluded)*

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## HISTORICAL FRAGMENTS.

### NO. 22. THE FUGGERS IN PORTUGAL AND SPAIN.[1]

BY EDWARD KREMERS.

Every American boy and girl will possibly recall that he or she learned in his or her United States History of a Portuguese Prince Henry whose cognomen was The Navigator. He or she will also remember that six years after Columbus had made his memorable voyage to the West Indies, a Portuguese, Vasco da Gama, circumnavigated the Cape of Good Hope and discovered the all water route to the East Indies. Thus, the Portuguese were the first to develop the spice trade by way of the new route. That the King of Portugal should levy a tax of 50 p. c. of all of the spices imported and that in 1505 he insisted on the sale of all spices through his officials in order that he might control the price does not seem surprising in the light of royal privilege.

In a previous account[2] it has been pointed out that Germany was the best customer of Venice, so far as the Levant trade of the Queen of the Adriatic was concerned, also that the import and export trade of Germany was largely in the hands of the Hanseatic merchants. When, therefore, in 1501 the war between the "Gross-sultan" and the Republic of Venice practically put a stop to the Levant spice trade (p. 22), the Fuggers, merchants of the Hanseatic city of Augsburg, made an attempt to establish trade connections with the Levant *via* Genoa. They had already collected at Genoa large supplies of copper in which they had a practical monopoly and which they intended to send to the Orient in exchange for spices, when the first spice-laden vessels arrived at Lisbon and thus pointed the way to a more convenient route for the importation of East Indian spices.

By August 1, 1504 the factor of the Welsers, Lucas Rem, had closed a contract with the King of Portugal which allowed them, together with Italian merchants, to participate in the fleet to be sent to the Orient. In the 1505 fleet the Italian merchants (Genoese & Florentine) participated with 30,000 cruzados. (Somewhat more than a ducat.) The Welsers alone participated with 20,000 ducats and the Fuggers, Hoechstetters, Imhofs, Gossenprotts and Hirschvogels together with 16,000

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[1] Gleanings from Konrad Haebler, "Die Geschichte der Fugger'schen Handlung in Spanien." Page references to Socialgeschichtliche Forschungen. (Ergaenzungshefte zur Zeitschrift fuer Social-und Wirtschaftsgeschichte.) Heft I, 1897. The figures in parentheses throughout the text refer to the pages of Ergaenzungsheft 7 and are inserted for the convenience of any one who may choose to verify the statements made or to seek additional information.

[2] Historical Fragments, No. 21: A German diarist in South America.

cruzados. Hence, the Germany Hanseatic merchants had a greater interest than the Italian merchants. How private initiative was interfered with by the crown has already been indicated.

That copper was taken to the Orient in exchange for spices has already been pointed out, also that the Fuggers possessed practically the European monopoly in this metal. It remains to be stated that some of their principal mines were located in Hungary, that the metal was taken by boat down the Weichsel to Danzig, the easternmost of the North Hanseatic cities on the Baltic, and thence *via* sea to Lisbon. These same ships also carried grain from Poland to the Iberian pensinsula. Moreover, since the Portuguese trade to the East Indies developed faster than Portuguese shipbuilding, many of the ships, especially the large ones, which were built at Danzig, carried a single cargo to Portugal and were there disposed of to merchants trading with the Orient *via* the new water route.

Pepper was the principal spice (hence pepperers) and we learn that the King of Portugal when, in 1505, he established a monopoly placed thereon a price of 22 ducats per cwt. (p. 22). We also learn that a certain Valentin Fernandez of Moravia, a printer, in 1514 had a charge of 700,000 reis for the printing of the Ordenaçoes do reino. Having business relations also with the German merchants, he accepted pepper for 400,000 reis and, no doubt, disposed of this spice to his German friends. It is definitely known that in the same year he thus disposed of 15 cwt. of cloves at 50 cruzados (@ 400 reis) to Michael Imhof and the Fuggers (p. 29). Again we learn (p. 30) that the King of Portugal, whose sister was married to Charles V, German Emperor, in 1527, offered (in 1521) to pay the dowery in pepper. 10,000 cwt. were to be delivered in Antwerp at the time of the September Fair (*Messe*) in 1521. He was to make two further deliveries to the Fuggers at New Years and Easter, 1522. We have previously learned (No. 20) that the Fuggers had been instrumental in the election of Charles as German Emperor and that the latter thus offered to meet part of his financial obligations to these Augsburg merchants.

The restrictions placed on private initiative by the Portuguese crown, as already pointed out, lead to a diminution of the Portuguese trade. Hanseatic merchants concentrated in part upon Antwerp (p. 24), in part upon Seville, Spain. In the course of time, the Fuggers maintained only a sub-factor at Lisbon who was subject to the factor at Seville. In 1558 the office at Lisbon was closed (p. 38). Indirectly, however, the Fuggers continued to do no small amount of business in Portugal. Thus, at one time (p. 40) they were in possession of Portugese notes to the extent of $15^1/_2$ million reis (= 40,000 ducats).

When Charles the fifth as Emperor of Germany in 1517 went to Spain, of which he became King as Charles I, having inherited the latter crown from his grandfather on his mother's side, *viz.* Ferdinand the Catholic, he was accompanied by agents of both Italian and German merchants. Thus, the Fuggers entered Spain, not *via* Portugal, but *via* the Netherland, *i. e.*, directly from Germany.

The Fuggers had maintained relation not only with the Emperor Maximilian, grandfather of Charles V on his father's side, but with the entire House of Habsburg. This, as well as the important financial rôle which Jacob Fugger had played in the election of Charles as German emperor, readily explains the presence of the agents of the Fuggers as well as of the Welsers when the young ruler went to Spain.

Though the Spanish Cortez tried to persuade Charles to burden the countries subject to the Habsburgs with the cost of his election as emperor, he could not avoid placing part of the burden upon Castille and Aragon in the form of Spanish concessions.

It was September 8, 1522, that the Victoria landed at San Lucar. She was the only one left of five vessels with which Fernão de Magalhaes (the Magellen of our U. S. histories) had set sail three years previously and had completely navigated the globe. Of commercial importance was the fact that she had discovered the Spice Islands for which Columbus had started out thirty years previously. It was claimed that these islands were outside the range of monopoly granted the Portuguese by the Pope. Though four of the vessels had been lost, the cargo of the remaining one paid not only for the cost of the entire expedition, but netted a small profit as well.

Plans were therefore perfected at once for a fleet to make the most of the new discovery. Although the Spanish spice monopoly had been restricted by the Cortes to Spanish merchants, the Germans were granted participation by the Emperor. As a matter of fact, of 16,000 ducats subscribed, 12,000 came from German merchants and of this amount 10,000 was subscribed by the Fuggers, thus giving them the privilege to send a private factor with the expedition who was to look after their special interests.

The full benefits of this East Indian trade, it was thought, could best be attained by making some port other than Seville the center of the spice industry. As already pointed out, Portugal, by its royal monopoly, had alienated individual enterprise. Most of the spices were transhipped to countries to the north. Antwerp and Brugges were the two principal ports in the Netherlands nearest the Atlantic. In order to compete with Portugal, Spain had to see to it that the German merchants would no longer have to sail by Lisbon to Seville in order to get their supplies. Coruña in Galicia was finally settled upon to be the Spanish spice port. In order to develop the new scheme, the Fuggers were requested to build a fleet of ships at Danzig and to deliver them with copper, naval stores and grain at Coruña. As in London, these men from the Baltic were known in Spain as *Esterlines* (Easterlings).

The next chapter deals with the farming out of the collection of rentals or taxes on the estates of three orders of which the King of Spain was grand master. It contains nothing about the spice or drug trade, but is mentioned here for the simple reason that the contents of chapter V, "*Almadine*," deal with a special phase of this monopoly granted the Fuggers, *viz.*, with the production and sale of mercury.

The mercury mines of Almaden belonged to the Calatrava order, one of the three referred to above. In all probability Spanish mercury was known to the Phœnicians, the Greeks and the Carthaginians. It is known that the mines of Almaden were operated by the Romans. During the period of the Visigoth invasion the mines appear to have lain idle. That the work was resumed by the Arabians becomes apparent from the name, for *Almaden* means the mine, *al* and *maden*. In common parlance, the mercury mines were differentiated by referring to them as *Almaden del azogue*. Gradually it overshadowed all other Moorish almadens to such an extent that the name became restricted to it. The castles of Almaden and Chillon together with their mines were presented to the Calatrava-

Order by Alfonso VIII, March. 27, 1168, and came at once under the immediate charge of the Grand Master.

It was not, however, until after the discovery of the production of the nobler metals by the amalgamation process that the mining of mercury ore and mercury acquired a new importance. Previously it had been used almost exclusively for the production of cinnabar as pigment. Although the only competing mines were those of Idria (in Krain, Austria), the demand for mercury and its compounds was not sufficient to warrant extensive mining operations.

Even before Ferdinand, the Catholic, became Grand Master of the Calatrava-Order, the mines seem to have been sublet. However, very little is recorded about their operation and the business conducted. One item records that a representative of King Ferdinand at the Portuguese court sold in 1508 several cwt., for which King John paid at the 5000 mrs. for mercury and 6000 mrs. for cinnabar.

Of special interest to us is the operation of the mines by the Fuggers from 1523, the year in which Charles V, or rather in his capacity as Charles I, King of Spain, farmed out to his German creditors the collection of the rentals in the estates of the three orders, to 1645, hence for more than a hundred years.

As previously pointed out, the Fuggers had acquired considerable mining experience in Tyrol. Whereas in a previous three-year period a Spanish contractor had netted 1,700,000 maravedís, the profits of the Fuggers was estimated at 2,200,000 maravedís. The Germans were reputed to be the best miners.[1]

The student of the history of commerce may well be interested in the details of the contracts between the King as Grand Master and the Fuggers. Suffice it here to point out once more that the Spanish advisers of the King naturally resented the invasion of the Germans in this field as well as in the transoceanic spice trade. Hence, at the expiration of the first three-year contract, the court made the attempt to transfer the lease to a Spanish contractor. The Fuggers, however, were prepared for such a possibility. They had in store not less than 2000 cwt. of mercury which they could place on the market in competition with that to be mined by the Spanish contractor.

The details of the mining operations may again interest the mining engineer, but scarcely the student of pharmaceutical history who is interested in mercury and its salts as items of the materia pharmaceutica. The latter, however, may be interested to learn how the metal was liberated from its ore. The mined ore was crushed to nut size, mixed with fine, moistened black ash and transferred to large earthenware dishes of special shape and these exposed to heat by direct fire.

The vessels were not filled completely. The mixture, spread out evenly, was covered with a layer of black ashes a finger in thickness so that a rim 2 to 3 fingers in width remained, in order that the sublimed mercury could condense on the cover of the vessel and deposit itself on the layer of ashes. Each vessel containing about

[1] This was true not only in Spain, but in the Spanish possessions as well. As late as the close of the 18th century Alexander von Humboldt states that every German who came to the colonies was regarded as possessing special knowledge of mining. This reputation the Germans had not only in Spain but apparently all over Europe. Thus the French explorers imported German miners to the copper districts of the Lake Superior region to develop mining operations. (Comp. Agricola **de re metallica** and Hoover's translation.)

27 lbs. of ore was closed with a convex cover rendered air tight by means of clay and placed in the furnace.

The furnaces resembled vaults of the height of a man. The vault-like roof had three rows of openings, six in each row. The vessels fitted into these openings so that the rim and cover were exposed. At times the covers also were covered with clay to render them air tight and to preserve heat. As a rule, the fire was started in the evening and the heat maintained for twelve hours. The freed mercury sublimed through the ashes and was deposited on the latter as liquid metal. After cooling the mercury was removed with iron spoons, washed and transferred to collecting basins in the magazines.

A furnace of 18 vessels accommodated 5 cwt. of ore and, according to the quality of the latter, yielded 30 to 80 or more pounds of pure mercury. The purest ore containing 50 p. c. mercury was not thus treated but, mixed with sulphur, exposed to heat to produce the finest cinnabar, the *vermellon excelente*, of which a yield of 50 p. c. of the ore was obtained.

Again the details of the technology, the pottery, the deforestation of the hillsides for fuel, the cost of operation, etc., do not concern us. Anyone interested in these details may consult the original from which the data of significance to the pharmaceutical historian have been gleaned. It may be mentioned, however, that during the contract period 1547–1550, 3761 cwt. $27^1/_2$ lbs. of mercury and cinnabar were sold, also 652 cwt. $98^1/_2$ lbs. of sublimate. Supplies remaining at the close of the period amounted to 2549 cwt. mercury, 691 cwt. cinnabar and 450 cwt. sublimate. If added these amounts would yield quantities greater than those produced during the quadrennium, for they apparently include the left-over supplies at the beginning of that period. The annual production has been computed from other figures at 650 cwt. mercury and cinnabar and 90 cwt. sublimate.

Only little of the mercury was sold in Almaden. The principal marts in the Iberian peninsula were Seville and Lisbon. Hence it may be assumed that most of the products were sold outside of Spain, though the Fuggers possessed the monopoly for that country. Thus the accounts of 1547–1551 reveal that 2188 cwt. of mercury and $465^1/_5$ cwt. cinnabar were shipped to Antwerp, Marseilles and Venice. The small gains on these transactions are explained by calling attention to the facts that 55 cwt. of both articles were lost in shipwreck, 1 cwt. was lost accidentally and 95 cwt. were captured by the French. Incidentally this brings out some of the dangers involved in the commercial transactions.

In 1550 the mines were ruined by fire and subsequently by flooding. That the Fuggers should have permitted the latter may again have been due to a policy, the details of which are of no pharmaceutical interest. Suffice it to point out that the succession of Philip II of Spain, who did not succeed his father as German emperor, naturally did not improve the status of the Germans in Spain. By way of explanation, it may be added that, whereas the Spanish crown was hereditary, the imperial crown was not and that it was the financial support lent Charles V by the Fuggers that had given these captains of industry, if this modern phrase be permissible, such a hold on Charles, not only as German emperor but as King of Spain.

Chapter VII bears the heading "Philip II, and the Fuggers (1563–1575)." It has already been pointed out that the Spanish did not love the foreigners, whether German or Genoese merchant princes, and that Philip II was inclined

to accede to the wishes of his counsellors to deprive them of their privileges. When in 1550 the mercury mine was destroyed by fire and subsequently flooded by water, the Fuggers availed themselves of the opportunity to reveal how indispensable they were. This was met by the counter move, the royal decree of 1560, which not only ended all contracts, in their original form, but practically wiped out the King's debts to the Fuggers amounting to about three million ducats.

In connection with the production of mercury, it has already been pointed out that it increased greatly with the discovery of the amalgamative process. As a rule, a certain Bartolomé de Medina of Seville has been pronounced discoverer of this process (p. 138). Apparently he first applied the process in the silver mines of New Spain, but he is not the discoverer. This becomes apparent from a letter of the *Audencia* in Mexico dated December 31, 1554 and addressed to Charles V and the Council of the Indies. In this letter it is reported that Bartolomé of Medina had come to New Spain with the complaint that the officers at Seville had refused the emigration of his German companion who understood the production of silver by means of mercury. Inasmuch as the new process was not only to improve the process of mining but also to increase the royal income therefrom six fold, the Emperor is petitioned to permit the migration of the German, whose orthodoxy seems to have been questioned, to Mexico (p. 138). Whether the petition was granted we are not informed. This much, however, we know that the amalgamation process was tried out successfully in Mexico in 1556.

During the thirteen years (1550–1562) during which the Fuggers did not operate the Almaden mines only 500 cwt. of mercury were produced. According to their new contract, the Fuggers had to produce 1000 cwt. annually (p. 142) and to turn over the entire amount to the government at the price of 25, later of 20, ducats per cwt. The government, in turn, sold the mercury in the ports of New Spain at 100 pesos (at 450 maravedis) per cwt. After two years the Fuggers produced 1200 cwt., later, 1500 cwt. and more. On 13,100 cwt. they netted $12^{7}/_{10}$ ducats per cwt.

On Jan. 1, 1573 the mining contract was renewed for another 10 years: The Fuggers were to furnish 1700 cwt. per year and to receive 30 ducats per cwt. (p. 146). In return for this renewal, the Fuggers were to give the government an immediate credit for one million ducats. The mining operations were improved to such an extent that the Fuggers were able to turn over the contracted amount of mercury during the first few months of the year, hence could produce a much larger quantity than stipulated by contract (p. 153). In this connection the author calls attention to one of the troubles the Fuggers had to contend with, one that had nothing to do with the animosity of the Spanish toward the Germans, *viz.* an industrial disease, the *Quecksilber sichtigkeit.* Operations were reduced during the hot months, hospital facilities were provided, convalescents were employed at other tasks, etc., but a complete remedy there was not. The student of the history of pharmacy would glean something about the medicaments employed, but on this aspect the author remains silent. The local archives rather than those of the house of Fugger may possibly shed light on this subject (p. 154).

In connection with the mercury operations, we learn that the Fuggers improved silver mining in Spain (p. 155), also that the introduction of the reverberation furnace enabled them to operate 40 cwt. of ore with the same amount of fuel that was formerly required for 7 cwt; with depletion of forests an important factor.

The balance of the chapter deals largely with the efforts on part of the Spanish Council to deprive the Fuggers of their concessions and finally with how the Fuggers made themselves indispensable to the King by loaning him 200,000 ducats to be used in paying the mutinous soldiers in the Netherlands.

Chapter VIII, entitled "Die spaeteren Jahre Philip's II," deals first with the climax of the house of Fugger and then with the beginnings of its downfall due to family dissensions in Augsburg. But little of special interest to the pharmacist may be gleaned. Thus we learn that during a decade 23,947 cwt. of mercury were produced representing a value of 700,000 ducats, half of which was net profit. We are also informed that a new twelve-year contract from 1582–1594 was signed; that the Fuggers were the bankers of the Spanish ambassadors, more particularly at the German imperial and the French courts and that advances of 100,000 ducats to these Spanish officials were regarded as something ordinary. Further that they did the banking business for other Spanish officials and that Cardinal Granvella trusted them more than either the Genoese merchant bankers or his own countrymen. Of international political schemes involving great sums of money that reveal the rivalry with the Dutch merchant marine and the early development of English shipping we are told, but inasmuch as these involve Polish grain to be sent to the Iberian peninsula and not spices, these accounts have but a general interest and involve nothing pertaining to the history of our materia medica.

The two remaining chapters afford even fewer pickings. We do learn, however, that between 1604 and 1614 as much as 39,416 cwt. of mercury, valued at 404 million maravedis were produced netting 166 million maravedis or 442,000 ducats, (p. 203) also that the expulsion of the Moors deprived the mines of some of their best workmen (p. 205). Again the attempt to take the mines away from the Fuggers in 1613 was not successful and according to the new contract they had to deliver 4500 cwt. annually in place of 3000 cwt. (p. 205).

The Fuggers had always paid their workmen every Saturday and that community depended on these regular payments. Philip IV at the beginning of his reign, made the attempt to regulate state finances by asking the Fuggers to assume responsibility for the monthly payroll of 50,000 ducats. In spite of their protests they had to assume this burden. The result was the ruin of the Spanish business. Before long they had borrowed $2^1/_2$ million ducats. Their assets were about as large but could not be collected from the government and others (p. 209).

A general summary in connection with the winding up of the Spanish affairs reveals the fact that from 1563 to 1641 the Fuggers delivered $253,154^1/_2$ cwt. of mercury to the government. Assuming that 1000 cwt. of mercury enabled the production of 1 million ducats of silver, the amount of mercury recorded corresponds to a silver production of 253,154,500 ducats of silver. Inasmuch as the government received the double tenth, *i. e.*, one-fifth thereof, its income from this source amounted to 50 million ducats. No wonder the Spanish kings refused to lend an ear to their counsellors who wished to deprive the foreigners of the control of the mercury mines. In 1639 another disastrous fire occurred in the mines. These were turned over to a royal manager in 1647 (p. 221). The new management did not produce as much as the Fuggers; it did not pay the workmen promptly, so these deserted. For a century the mine produced but little. It was only when taken over by the Rothchilds that the former output was again reached.

# THE DEPARTMENT OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY

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| Connecticut | Maine | New Mexico | Utah |
| Delaware | Maryland | North Carolina | Vermont |
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| Illinois | Missouri | Pennsylvania | Wyoming |

## LEGISLATIVE NEWS.

Three more states have been added to the prerequisite list at the winter's session of the legislatures. Colorado, Kansas and Texas are to be congratulated, first, on their hard work in fighting for this legislation, second, on their success. This makes a total of 36 states and the District of Columbia with laws requiring college training. The other twelve states should start work now for the next session of the legislatures. There is a possibility of still adding another state or two this year as some of the legislatures are still in session and bills are pending.

**Arizona.**—Secretary Hulett reports that H.B. 95 is now law. Any place of business using the words "drugs, drug store, pharmacy" or others of like import must be in active charge of a registered Arizona pharmacist.

**California.**—The Supreme Court has rendered an opinion that the Board cannot revoke the license of a pharmacist when an inspector finds the store is not in charge of a licensed pharmacist. The lower tribunals had ruled to the contrary. In this particular instance, the Board had charged three violations and therefore revoked the license of the owner of four chain stores. Similar decisions have been previously rendered in other states and for that reason it is deemed better to "suspend" a license indefinitely or for a stated length of time, at the end of which it can again be suspended.

**Colorado.**—*Good news.* Two out of three bills passed, the successful ones providing for the college prerequisite and an increase in the store license fee from 50 cents to $5.00. The third bill, providing for the sale of drugs in original packages in places where there is no licensed pharmacy, was burdened with an unfortunate amendment and, therefore, allowed to die in committee.

Colorado is to be congratulated on its persevering and constructive fight for the legislation it wants. At the previous sessions of the legislature, a very good and complete pharmacy law was introduced, which failed in passage because of the combined opposition to several minor features. This year, the legislative workers studied the problems presented, and using the old pharmacy law as a basis, proposed a few important amendments, concentrating on these, and the result is success. Had the three provisions been combined into one bill, it would have been necessary to accept the broad construction on the sale of packaged goods everywhere or else lose the prerequisite. By separation, it was possible to drop the objectionable amendment without losing the college prerequisite amendment.

**Connecticut.**—The druggists of Connecticut are preparing to introduce a measure in the legislature which would do away with the college graduation exemption in the law and make it necessary for *all* candidates who take examination in the future to be college graduates regardless of when they entered the profession.

If proposed drafts of laws were made so as to limit exemptions from graduation, as provided for in the N. A. B. P. model law propositions, it would not be necessary to correct such omissions later, by amendment.

**Kansas.**—The good news has been received that House Bill 162, which is the college prerequisite bill, has passed both houses and will become the law when published in the statutes, which will be about July 1st. It wasn't an easy struggle either, as there was opposition from several strong sources, but that only adds to the glory of the proponents who were willing to fight to the last ditch.

**Maine.**—With organized pharmacy fighting for prerequisite legislation in nearly every state without the college provision, the Maine Pharmaceutical Association is opposing a bill introduced by an outside source which provides for college of pharmacy graduation as a prerequisite to examination. Its objection is based on two reasons; the first, that the standard was raised to high school last year, and the second that there is no college of pharmacy in the state.

The answer to the first objection is practice in other states. Most of the prerequisites enacted have jumped standards from grammar school education to college of pharmacy graduation, witness Colorado this year. At this late date when thirty-seven states are on a prerequisite basis, it is necessary to take a big jump to get in line, otherwise Maine pharmacists as well as those of other non-prerequisite states will find themselves barred from practically every state as far as reciprocity is concerned.

The fact that there is no college of pharmacy in the state should not deter the enactment of a prerequisite, inasmuch as the N. A. B. P. model law, which should be followed if possible, provides a five-year exemption period for those in the business at the time of passage. The state would not be on a strictly prerequisite basis, therefore, for a period of five years. In the meantime, a pharmacy department could undoubtedly be put into the state university. The University of Maine has probably been obliged to postpone the establishment of a pharmacy department for years because the state law did not require college training in pharmacy.

One of the progressive pharmacists of the state, Edgar F. Carswell, former secretary of the Maine Board, introduced a resolution at the meeting of the Maine Pharmaceutical Association in Augusta, on Feb. 14th, which was adopted, requesting the University of Maine to establish a pharmacy department and appoint a committee to go into the matter with the trustees. Perhaps there is hope for next time.

**Maryland.**—A number of bills have been introduced in the legislature without the authority or approval of the Maryland Pharmaceutical Association or Board of Pharmacy. Secretary Swain reports, however, that it is improbable that any of them will get out of committee.

House Bill No. 280 would repeal assistant pharmacist registration and grant *full* registration without additional examination to every assistant pharmacist upon expiration of five years from date on which he was registered. Note that the expiration of five years, not pharmaceutical experience after registration, is specified under this provision.

House Bill No. 312 would permit operation of drug store in towns of 3000 or less without a registered or assistant pharmacist in charge, requiring registered help only for filling prescriptions and dispensing poisons. Fortunately it died in committee.

A bill reducing license fee for itinerant vendors, a caustic acid and alkali bill with unfortunate definitions, and an anti-vivisection bill which would prohibit the use of dogs and would therefore prevent certain types of official assaying—all died in committee.

**Massachusetts.**—A law pending before the legislature provides as follows: "No registered pharmacist shall sell any patent or proprietary medicine which contains more than six per cent of alcohol, except upon the prescription of a registered physician." It is evidently intended as a check on the sale of wine tonics, etc. The provision is foolish, however, as strictly enforced it would prohibit the sale of practically any proprietary medicine without a physician's prescription.

**Minnesota.**—Several bills affecting pharmacy are pending in Minnesota. One provides for an increase in renewal fees from $3.00 to $5.00, the purpose being to provide funds for an analytical laboratory and otherwise to aid the board of pharmacy in its work. The second amend-

ment corrects the college prerequisite clause which now requires only two years of attendance at a recognized college of pharmacy and will be changed to read that the applicant must be a graduate in pharmacy. The three-year course necessitated this change. The third amendment provides for discontinuance of the assistant examination after January 1, 1930, but permits all assistants so registered before that time to continue as such.

**Montana.**—J. A. Riedel, secretary of the Montana Board of Pharmacy as well as of the state pharmaceutical association, has sent out a notice urging against passage of Senate Bill 133 which would permit any person to dispense prescriptions within a hospital upon written order of a licensed physician. Smaller hospitals and institutions could dispense with the services of a registered pharmacist and the lives of patients would be imperiled, as inexperienced help could be used to fill prescriptions.

**New Jersey.**—Senate Bill 17 amending the pharmacy law was signed by Governor Morgan F. Larson on March 25th. The examination fee of registered and assistant pharmacist is raised from $10.00 to $25.00, and annual instead of biennial re-registration is required, the fee being $2.00 annually instead of $1.00 biennially. The entrance requirements for assistant examination have been raised, making it necessary to show proof of at least two years of successful work in a recognized school of pharmacy.

**North Dakota.**—Senate Bill 71 has been passed by both houses and is awaiting the signature of the governor. It corrects the pharmacy law to permit pharmacy graduates to write examination in the theoretical subjects immediately upon graduation and return later to take the practical work when all the requirements have been fulfilled. Heretofore this has been impossible under the law; evidently an outcome of the discussions of this subject at the last two N. A. B. P. conventions.

**Oklahoma.**—Secretary Anderson writes, "The regular session of the legislature is about to adjourn and our pharmacy bill no doubt will die on the calendar. However, we shall make another attempt in the extraordinary session, which will be called about April 15th." The bill was of the drug store designation type.

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## PERSONAL AND OTHER NEWS.

**H. L. Haussamen,** of Grafton, N. D., veteran member of the North Dakota Board of Pharmacy, we are informed, is very critically ill, having suffered a stroke causing loss of speech and paralysis of one side of his body. Mr. Haussamen had been ailing for some time and is under a physician's care, but until recently his condition was not considered serious. He has been an active worker in the N. A. B. P. since its organization, and his many friends are hoping to hear soon that he is on the road to recovery.

**George Judisch,** member of the Iowa Board and N. A. B. P. vice-president, was honored with the presentation of a diamond stick pin at the recent state pharmaceutical convention in Iowa, for his splendid services as chairman of the Legislative Committee for the last twelve years.

**Miss Marie Piesinger,** of Northfield, Minn., one of the few women serving on boards of pharmacy in the country, has been honored with a life membership in the Minnesota Pharmaceutical Association recently. She is the first woman upon whom this honor has been bestowed.

District No. 3 announces that a joint meeting of the colleges and the boards in the district (Illinois, Indiana, Wisconsin, Michigan, Kentucky and Ohio) will be held at the Hotel Statler, Detroit, Michigan, Tuesday and Wednesday, April 23th and 24th. Chairmen J. A. J. Funk for the boards and Roland T. Lakey for the colleges will be in charge.

The annual reports of two boards of pharmacy are acknowledged—Iowa and New Jersey. Both give a complete financial statement as well as a list of the pharmacists practicing in the state with license number and address. The Iowa copy is cloth bound for the biennial period ending June 30, 1928. The New Jersey report comprises the February–March issue of the "New Jersey Journal of Pharmacy." Such information is of great value to the N. A. B. P. central office and is appreciated.

## STATE BOARD NEWS.

**Alabama.**—Secretary Bingham writes that the Alabama Pharmaceutical Association is busy giving relief to eleven druggists in southeastern Alabama who have been wiped out by the flood, suffering a loss of about $80,000. The association is trying to raise a minimum of $20,000. Some druggists have been wiped out completely, losing household goods and personal possessions as well as the entire store. A telegram was sent out promptly to every druggist in the state asking for immediate aid.

**Arizona.**—The new governor, John C. Phillips, recently appointed two new members to the board of pharmacy—Arthur Lee Phelps, of Phoenix and M. J. Nicholson, of Willcox.

**Colorado.**—The results of the December examination published recently show as follows: That of 47 candidates for the registered pharmacist certificate, 30 were successful (nearly 64%) and that 27 of the 40 contenders for assistant registration also were granted licenses.

Morton R. Smidt, of Iowa has been granted reciprocal registration.

Announcement is made of an examination in Denver on May 17th and 18th. Address inquiries to Arthur D. Baker, secretary, 228 State Capitol Bldg., Denver, Colo.

**Illinois.**—Reciprocal registration has recently been extended to the following: James S. Mason, of Arizona; I. E. Eber, of Colorado; Keith M. Clifton, B. B. Lehman, Mora A. Lindquist, Wm. C. Gardiner, Jr., Harold R. Eaton and True H. Wengert, all of Iowa; Frank C. Clark, of Michigan; E. O. Grabruck and James Garrett, both of Missouri; R. A. Anderson, of Rhode Island; and Sister Leonissa Woletz, of Wisconsin.

**Indiana.**—B. M. Keene recently resigned as a member of the Indiana Board, as his business interests will demand more of his time than in the past. Mr. Keene served as a member of the Board for six years and has a record of never having missed a single meeting. He was appointed by Governor McCray in May 1923, and re-appointed by Governor Jackson in May 1927. On both occasions, he was endorsed by the Indiana Pharmaceutical Association. He has been very active in N. A. B. P. work having served as vice-president and chairman of District 3 as well as working on many committees. His colleagues on the board express regret over his decision to resign, as he has been a valuable member.

Scott Kelly, of Gaston, has been appointed as Mr. Keene's successor. He is a Purdue graduate, class '06, past-president of the Indiana Pharmaceutical Association, and the appointment meets with the approval of Indiana pharmacists.

Reciprocal registration was granted during March to Henry Aumann, of Illinois, and Frank F. Neal, of Ohio.

**Iowa.**—An important victory has been won in the fight to prevent the sale of aspirin by others than pharmacists. A recent decision of the District Court upholds the state board of pharmacy in restricting the sale in this manner. In order to enforce the ruling, a Supreme Court decision will be necessary and this test case will be appealed immediately for that purpose.

**Kansas.**—The date of the next meeting of the Kansas Board of Pharmacy has been set for June 12th and 13th, to accommodate students of the schools of pharmacy and permit them to finish courses before taking examination. Place is given as Lawrence.

**Kentucky.**—An interesting experiment in law enforcement is being tried by the Kentucky Board. Instead of taking a violator to the criminal courts and having him fined a small amount of money, paying the fine and going back to his business to continue the same offense, in this particular case, being the operation of a drug store without a registered pharmacist in charge, the Board has taken the matter to the civil courts and asked an injunction restraining the defendant "from forever hereafter, or until he is duly and legally licensed and registered so to do, or until he employs a pharmacist registered under the laws of the state of Kentucky from practicing pharmacy or conducting or operating a drug store, etc." If the court upholds the Board and grants injunction, law enforcement will be made more effective. It is easy to pay a fine but hard to take the choice of closing up a place of business or operating it at all times in accordance with the law. Pharmacy will be made unprofitable to violators and therefore unattractive.

The results of the examination held in Lexington on February 12th show nine out of twenty-two applicants for registered pharmacist certificate successful and seven out of ten for the assistant certificate.

Reciprocal registration was granted to Julius T. Toll, of Ohio; Curtis H. Duke, of Georgia; Joe H. Triplett, of Ohio; Joseph E. Maupin, of Illinois; and William L. Claxon, of Indiana.

George Wilhelmi, of Newport, qualified as the newly appointed member of the Board; he succeeds Albert E. Ely, whose term expired recently.

The following officers were elected for the ensuing year at the annual meeting: *President*, William Votteler; *Secretary*, J. W. Gayle; *Treasurer*, Linwood A. Brown; *Chairman Executive Committee*, George D. Duncan.

The results of the examination held in Owensboro on April 9th will be published later.

**Maine.**—George O. Tuttle, of 419 Congress St., Portland, Maine, has been made secretary of the Board, the office held by Edgar F. Carswell before his retirement a short time ago.

An examination meeting was held in Augusta on February 13th and two out of eleven candidates were successful, having been granted licenses as registered pharmacists. Herbert C. Eggleston was granted license by reciprocity on the basis of Vermont registration.

**Maryland.**—Reciprocal registration was granted on March 8th to J. Webster Merritt, of Florida.

**Massachusetts.**—The following results of examinations have been published recently: Out of a class of 60 examined December 11th, 20 were granted licenses as pharmacists; out of a class of 62 examined on January 22nd, 27 were successful.

Reciprocal registration has been granted to M. Kevorkian and John W. Lowe, of Connecticut.

**Michigan.**—Reciprocal registration was granted during March to Henry J. Hachen, of Georgia; Clarence C. Hill, of Indiana; Paul C. Cussen, of Ohio; James L. Allen, of Tennessee; Jacob Kessler, of Vermont; and Harold V. Lysaght, of Wisconsin.

**Minnesota.**—At the annual meeting the Board held recently, J. P. Jelinek was elected president and John W. Dargavel was reëlected secretary.

**Mississippi.**—Reciprocal registration was granted recently to T. A. Bourland, of Alabama.

**Missouri.**—The regular examination was held on April 8th and 9th at the Kansas City College of Pharmacy, Kansas City, Mo. Results will be published later.

Thomas Larsen, of Nebraska, was granted a license by reciprocity in March.

**New Jersey.**—The Board of Pharmacy announces the following results of the written examinations held at the State House, Trenton, N. J., on January 17th and 18th: Ten applicants who had previously passed the examination in Practical Work completed the written work successfully and were granted certificates of registration.

A total of 122 applicants took the written examinations; of these 42, or about 34%, were successful in the written work. The balance were successful in one or more of the written tests, but not successful in all four.

Two applicants who had previously passed the examination in Practical Work for "assistant pharmacist" completed the written work successfully and were granted certificates as "assistants." A total of 48 took this examination. Of these, 22 or about 46% were successful in the written work. The balance were successful in one or more of the written tests but not in all four.

On February 19th, Governor Larson announced the appointment of W. Scott Taylor, Jr., to succeed William H. McNeill of Midland Park. Mr. Taylor's appointment takes effect June 1, 1929.

Reciprocal registration has been extended to Kirk Smith, of Delaware and A. H. Martin, D. R. Everitt and Samuel Dezenhall, of Pennsylvania.

**New Mexico.**—An examination meeting will be held at the Franciscan Hotel, Albuquerque, New Mexico, on May 20th.

Mortimer Levine, of Pennsylvania, was registered by reciprocity in March.

**North Carolina.**—The next meeting of the North Carolina Board of Pharmacy for examination of applicants for license to practice pharmacy both as pharmacist and assistant pharmacist will be held at Chapel Hill, June 11, 1929, at 9 A.M. For information, write F. W. Hancock, Secretary, Oxford, N. C.

Reciprocal registration has been extended to John F. Sutton, of South Carolina, and Garrett E. Andes and William E. Armstrong, of Virginia.

**Oregon.**—The board of pharmacy will hold its meeting for the examination of applicants as registered pharmacists beginning Tuesday, June 4, 1929. The meeting will probably last for three days and will be held simultaneously in Corvallis and Portland.

Frederick M. Christensen, of Utah, and Albert H. Dewey, of Washington, were recently granted reciprocal registration.

**Pennsylvania.**—Reciprocal registration was recently granted to the following: Warren A. Walton, of Colorado; Arthur C. Thorsen, of Illinois; Armand M. DuPaul, of Massachusetts; Joseph Robbins, of New Jersey; Jack M. McLaughlin, of North Carolina; Oswald V. Todd, of Washington.

**Rhode Island.**—James A. Kennedy, of Massachusetts, was granted reciprocal registration on March 18th.

**South Carolina.**—George D. Padgett, of Georgia, was granted a license by reciprocity on March 21st.

**South Dakota.**—Secretary W. P. Loesch recently announced that five out of a class of fourteen candidates examined in Mitchell in November have been admitted to full registration.

**Texas.**—Forty-six applicants recently passed the examination and will be given licenses in the words of W. H. Cousins, secretary, "to practice the ancient and honorable apothecary's art." Sister Mary Finian Bradley and Sister Rasario Terry tied for the highest average, $86^{2}/_{3}\%$.

Reciprocal registration has recently been granted to the following: William B. Gould, of Arkansas; Frank H. Martin, of Colorado; James W. Minus, of Florida; George L. Kramme, of Iowa; Howard L. Sandoz, of Louisiana; Thos. M. Bailey, of Missouri; Owen P. Lindley, of New Mexico; Walter H. Owen, of Ohio; Erich B. Fritsch, of Wisconsin.

**Vermont.**—O. W. McShane, of Poultney, has been appointed a member of the Vermont Board to fill the vacancy caused by the death of F. W. Churchill, of Proctor. As Mr. McShane has previously served on the Board, he is well prepared for the work.

The annual meeting of the Board was held on February 6th and the following officers were elected: *President*, Ralph C. Root; *Treasurer*, H. W. Alexander; *Secretary*, Fred D. Pierce. Secretary Pierce is also the Hon. Fred D. Pierce, as he is the member of the House of Representatives from Barton.

**Virginia.**—H. C. Littlejohn, of Leesburg, has been reappointed to the Board of Pharmacy for a term of five years beginning March 1, 1929. Mr. Littlejohn has been vice-president of the Board for some years.

The annual meeting of the Board will be held in Richmond on April 23rd. Election of officers will take place at this meeting. Examinations will be conducted in Richmond on June 4th and 5th.

**Washington.**—Reciprocal license has recently been granted to Carl E. Robinson, of Nebraska.

**West Virginia.**—Reciprocal registration was recently granted to the following: P. A. Prioletti, and Geo. A. McLean, both of Pennsylvania; Virginia C. Ellis, James H. McNeer, Jr. and Cabell B. Carlan, all of Virginia.

**Wisconsin.**—Of 130 candidates who took the quarterly examination given by the Board of Pharmacy at Madison, 55 were successful in passing. The large number of candidates is probably due to the fact that exemption from the college graduation requirement expires in 1930.

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## AN OLD APOTHECARY SHOP OF ROME.

It is said that Dr. Recole Scalleta, 84 years of age, has been for 62 years apothecary in the Plaza delia Maddalena of Rome. The apothecary shop is located in an old section of the city and is said to have been founded in the 16th century by monks and operated under such auspices until the establishment came into the possession of the Prato family about two hundred years ago. An historical account describes the shop furniture and equipment as of different periods during which this venerable establishment has served its patrons; some of its fittings and fixtures having been on terms of acquaintance with the dust of several centuries.

# THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

The teaching of pharmacy subjects is receiving considerable attention by professors of pharmacy. The recent articles by Professors Cox and Cook and the present one by Professor Briggs show the deep interest taken by teachers of pharmacy in the subjects. Comment on these three papers is invited.

C. B. JORDAN, *Editor.*

## THE TEACHING OF DISPENSING PHARMACY.

BY W. PAUL BRIGGS.*

The article of Professor Cox in the November JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION touched upon a point of great interest to me and I believe to all other teachers confronted with the task of teaching Dispensing Pharmacy under the handicaps imposed by the absence of adequate apprentice training. I have worked out a plan which has been tried this year and the results are so gratifying that I feel it may be of interest and, possibly, some small value to others who are so situated.

The background for the Dispensing Course is, as in most schools, a thorough course in the theory and manufacture of the preparations of the U. S. P. X and N. F. V. This along with General Chemistry, Botany and general cultural work constitute the first year. Beginning with the second year (not considering the usual allied subjects) the students study an approved treatise on Compounding and this is correlated with work in the laboratory. Here we use a mimeographed manual of Prescriptions in which I have attempted to present all the various types of prescriptions, grouped as, Mixtures, Solutions, Liniments, Powders, Capsules, Pills, Tablets, Konseals, Plasters, Ampuls, etc. Under each heading I have given typical formulas and complete directions for compounding, principally to teach technic. After preparing several simple solutions, for example, the student then compounds others involving special manipulation, in each case receiving specific directions for the method to be followed. This same plan is followed throughout the various groups of prescriptions and totals about 100. In other words we give directions for preparing each type of prescription without stress upon incompatibility, and along with this the instructor's personal attention developing accuracy, acumen, proper packaging, labeling, prices, etc. This consumes the first semester's work.

For the next two months of the following semester the students compound prescriptions involving incompatibilities, without directions for preparing, and are expected to apply principles brought out in the first semester. All prescriptions must be checked by another student and his initial must be on the prescription. Should a prescription be turned in which is unsatisfactory in any way the student

* George Washington University.

checking as well as the compounder lose credit and the prescription is returned and must be prepared again. This has developed a degree of accuracy which I had never been able to attain before. It involves additional work for the instructor but the results amply pay for the effort. All prescriptions are numbered, labeled, capped and dispensed just as in a professional pharmacy. Below each prescription in the manual is sufficient space in which the student briefly discusses the work, and to the left of the ingredients the students use brackets and numbers to indicate the order of mixing. This makes grading of notebooks very simple and some students report that this system of numbers and brackets has been adapted in actual practice, as it requires but a moment and leaves definite instructions to the next pharmacist who compounds the prescription.

From this point prescription work is dropped and the student receives an applied course in qualitative analysis for the remainder of the term.

Beginning with the third year we resume the compounding, but this time from a different angle. From many thousands of prescriptions on the narcotic files of pharmacies located at widely separated sections of the city and suburbs I selected enough of the most useful and typical to bind 50 prescriptions in a book and allow one book for each student. These books are lettered A, B, C, etc., and the prescriptions numbered 1 to 50. These books are rotated among the students so that each student copies or compounds nearly 1000 original prescriptions, assuming the class to be composed of 20 students. This means typical, modern prescriptions in the physician's handwriting without modification—in some cases ambiguous, blurred, crumpled, incompatible, toxic doses, incompatible proprietaries, etc. This course runs for one semester with 2 lectures or recitation periods and 2, 3-hour laboratory periods per week. We begin by having the students copy the prescriptions, changing the quantities to the other system in which it is written, changing synonyms to official titles and official titles to synonyms, translating the directions to household measures and giving the method of compounding. Each student can complete about 8 prescriptions in this manner in a 50-minute period and leave enough time to discuss the previous lesson's work. By using the total 8 hours per week for the first few weeks each student studies about 100 such prescriptions and then the work is transferred to the laboratory where prescriptions in books other than those copied are actually compounded. The class periods now are utilized to point out peculiar phases of penmanship and ways to interpret directions and ingredients from a study of the prescription as a whole. In fact this class carries itself, as the instructional possibilities in dealing with the actual prescription are unlimited. Further, the interest of the students is so keen that if they could they would take this course to the exclusion of all the others.

It has been aptly said that, "To teach John Latin you must not only know Latin but you must know John." Likewise when you can arouse interest in John for Latin you can teach John Latin. Planning these courses and carrying them out require time and effort but the enthusiasm of the students has more than repaid me for the effort. And more—the students learn and retain. What more could an instructor ask?

There is much room for improvement and I would welcome criticism that will be of mutual benefit to all concerned with this paramount subject.

# COMMITTEE REPORTS

## COMMITTEE ON STANDARDS OF DRUGS AND CHEMICAL PRODUCTS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

BULLETIN I—1928-29.

BY. E. N. GATHERCOAL, *Chairman.*

Upon assuming the chairmanship of the Committee on Standards of Drugs and Chemical Products, an impulse led me to a short study of the history of this Committee during the twenty years of its existence. Its origin, personnel, activities and accomplishments have proved of such interest to me that I have compiled the items noted and have laid the whole before President Jones of the A. PH. A., as well as the membership of the Committee, Editor Eberle and Secretary Kelly.

The Committee was first known as the Committee on Standards of Non-Official Drugs and Chemical Products. Later, the word "Non-Official" was dropped from the title. These names have been shortened to "Committee on Unofficial Standards and the Committee on Standards."

### ORIGIN OF THE COMMITTEE.

At a meeting of the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1908 at Hot Springs, Arkansas, Dr. J. H. Beal presented a Resolution (Exhibit "A" in the Appendix) and moved its adoption, that the A. PH. A. form a committee to be known as the Committee on Standards of Non-Official Drugs and Chemical Products and consisting of fifteen members to be elected by the Council. This motion was approved and the Committee was elected at a subsequent meeting of the Council at Hot Springs.

### CHAIRMEN OF THE COMMITTEE AND COMMITTEE PERSONNEL.

George M. Beringer was appointed chairman of the Committee in 1908 and served until his resignation was accepted by the Council at the Atlantic City meeting in September 1916. Dr. J. A. Koch subsequently was elected by the Council to serve as chairman of this committee and fulfilled that office until his resignation in February 1921. In July 1921, Dr. B. L. Murray was elected chairman and served until September 1928. Thus the twenty years of service of this committee has been directed by three chairmen, each serving, approximately, the same number of years.

It is to be noted that of the fifteen members of the Committee elected by the Council in 1908, four, namely, Messrs. Beringer, Koch, Puckner and Raubenheimer, have served for the full twenty years. Thomas P. Cook served until his death, in 1911, and John M. Francis for seventeen years until his death, in 1924. Geo. M. Beringer died in 1928 in his twenty-first year of service. Messrs. J. A. Koch and Otto Raubenheimer are still members of the Committee. George D. Rosengarten has served 19 years and Henry Kraemer for 16 years until his death, in 1924. From 1917 to 1924 inclusive, there was no change in the personnel of the Committee. In 1925, President Holton reappointed but 12 members of the Committee. Messrs. Francis and Kraemer had died, in 1924, and Messrs. Beringer and Eldred are here considered as retaining their places on the Committee. The full membership of sixteen was restored in 1926. The full roster (Exhibit "B" in the Appendix) of the Committee for the twenty years embraces 37 very prominent names in the recent history of the A. PH. A.

### ANNUAL REPORTS OF THE COMMITTEE.

Chairman Beringer's first report was made at the 1909 meeting. A brief summary of the report, stating the purpose of the Committee and the resolutions authorizing its appointment, is as follows: "To prepare from existing sources of information a tentative list of the principal drugs, chemicals and medicinal preparations not recognized by the U. S. P., with a suitable system of nomenclature for the same, and to adopt suitable limits of strength and purity therefor."

The Committee presented a tentative list which included 37 drugs of animal origin, 27 of mineral origin, more than 500 of vegetable origin, over 200 pharmaceutical preparations and

about 600 chemicals. It is admitted, in the report and in the discussion, that the list is entirely too voluminous. No monographs nor standards were submitted; however, certain principles and methods were worked out by the Committee for its guidance and the permanent continuance of its work, which were, later, adopted by the Council, and may be summarized as follows:

The Chairman shall conduct the business of the Committee through bulletins which shall be issued, if practicable, semi-monthly. All business shall be presented in the form of written motions which, after a suitable time for discussion, shall be balloted upon by mail and, ordinarily, the majority of the votes cast shall decide the question. Products adopted by vote shall be assigned to individual members for report and recommendation. Titles, purity rubric and methods of testing shall follow the style of the U. S. P. monographs and other rules governing proprietary products, medicinal uses and doses; chemical formulas and molecular weights, botanical nomenclature, etc., are included. (See PROC. A. PH. A. (1909), 501–520 incl.)

The second report by Chairman Beringer, made in 1910 at the Richmond meeting, stated that six bulletins had been published during the year; a meeting of the Committee had been held at Richmond and a selection of articles to be standardized had been made by the Committee. The preparation of a number of tentative standards had also been accomplished. This report also discusses the results, (p. 515) regarding coöperation between the Committee of Pharmacy and Chemistry of the A. M. A. and the Committee of Non-Official Standards of the A. PH. A. Messrs. Beringer, Caspari and Francis were reëlected to the Committee; C. A. Dye was elected in place of Geo. B. Kauffman, resigned, and H. H. Rusby was elected a new member. (PROC. A. PH. A. (1910), 514–519.)

The report of Chairman Beringer, in 1911 (BULLETIN, A. PH. A., 591–595) indicates that coöperation of the Committee with the N. F. Committee has been requested. Also the Committee on Unofficial Standards had requested the coöperation of the Department of Agriculture and the Treasury Department of the United States in its work. A large number of tentative monographs had been prepared and a request was made of the Council that these be published in the new JOURNAL A. PH. A. for criticism, which was granted. During 1911 the Committee lost E. Ladish, by resignation, and Leo Eliel, by death. The new members elected to the Committee were: B. L. Murray, F. R. Eldred, L. D. Havenhill and E. L. Newcomb.

During 1912, sixty-two monographs were published in the JOURNAL. The report of Chairman Beringer indicates that a large amount of work was in progress (see JOUR. A. PH. A., pp. 67, 161, 1104).

The report of Chairman Beringer in 1913 indicates that the work had slowed up, due to the fact that so many of the members of the Committee were actively engaged in U. S. P. and N. F. revision work. However, the Committee was still actively at work in the preparation of monographs for the N. F. and 46 monographs had been published in the JOUR. A. PH. A. (see pp. 248, 369, 519, 1074 and 1514).

In 1914, forty-four new monographs, prepared by the Committee, were published in the JOUR. A. PH. A. (see pp. 873 and 1597). The report of Chairman Beringer (see p. 1397) indicated very satisfactory progress in the work of the Committee.

In 1915, sixty-eight monographs, prepared by the Committee, were published in the JOUR. A. PH. A. (see pp. 632, 751, 1131 and 1378). The report of the Committee by Chairman Beringer is printed on p. 1255.

In 1916, seven new monographs, prepared by the Committee, were published in the JOUR. A. PH. A. (see p. 861). The extended report of Chairman Beringer will be found on p. 1276. Nearly 300 drugs have been considered by the Committee and 227 monographs have been published. Practically all of the monographs in Part II of the N. F. IV and eleven U. S. P. IX monographs represent the work of this Committee. About 30 monographs were published that were not made part of the N. F. nor U. S. P. He suggested that the standards prepared by the Committee should be submitted to the Committee on Standards of the Association of Official Agricultural Chemists and of the several associations representing the wholesale drug trade and manufacturers of pharmaceuticals and chemicals so as to insure their acceptability and correctness as far as possible. The Council approved the motion that the monographs of drugs already prepared and that might be prepared in the future should be published in the JOURNAL OF THE ASSOCIATION, so that when sufficient material has accumulated the monographs may be published as a book of standards under the control and authorization of the AMERI-

CAN PHARMACEUTICAL ASSOCIATION. The Council reëlected the members of the Committee whose terms had expired (p. 128). Mr. Beringer was reëlected Chairman for the ninth time but, because of the pressure of other work, asked to be excused from serving again as Chairman. Dr. J. A. Koch was elected in his stead. Mr. Beringer's splendid work as chairman of this Committee and on the N. F. Committee was suitably recognized (p. 1285).

Chairman Koch's first report, in 1917, indicated that the work of the Committee had been continued, forty topics had been assigned and accepted for report by members of the Committee. The Chairman indicated that the Committee should now work on drugs and chemicals not contained in either the U. S. P. or N. F., thus coming back to the original purpose for which the Committee was formed (see JOUR. A. PH. A., p. 1101).

In 1918, Chairman Koch reported that owing to the present conditions due to the War, work on the formulation of standards had been much impeded. Standards for a considerable number of products were still under consideration (see p. 912) and for three products standards had been tentatively adopted.

In 1919, Chairman Koch stated that the work of the Committee had been practically at a standstill for the greater part of the past year. Monographs for two articles are included with the report.

In 1920 no report of the Committee is found in the JOURNAL, A. PH. A.

In February 1921, Dr. Koch resigned as Chairman and Dr. B. L. Murray was elected to the office by the Council in July 1921. Dr. Murray's report indicated one monograph completed and fourteen in progress of study (see JOUR. A. PH. A., p. 800).

In 1922, Chairman Murray reported that the Committee had brought no standards to completion during the year. Numerous standards were prepared in tentative form (p. 842).

In 1923 no report of the Committee is found in the index of the JOURNAL.

In 1924 the report of the Chairman indicated that no monographs had been prepared as the members of the Committee are still actively engaged in the revision of the U. S. P. and N. F. (p. 954).

In 1925 no report from the Committee is found. The appointment of this Committee is placed with the President of the ASSOCIATION by action of the Council, pp. 263–4. No report was made in 1926.

In 1927 (see JOUR. A. PH. A., p. 998) a short report by the Chairman indicated that the Committee is now ready to resume its activities which were for a time curtailed by the active revision work in connection with the Pharmacopœia and National Formulary. Coöperation with the botanical committees of the National Conference on Pharmaceutical Research was effected and the hope was expressed that greater efficiency would be obtained through such coöperation.

The 1928 report by Chairman Murray was submitted in Portland, Maine, and published in the JOURNAL in January 1929. It indicates that four monographs have been completed, three more are practically completed and twenty-six more are in the process of preparation.

FINANCES OF THE COMMITTEE.

From the reports of the Treasurer of the A. PH. A.

| Year. | Appropriation. | Amount spent. | Year. | Appropriation. | Amount spent. |
|---|---|---|---|---|---|
| 1908 | .... | .... | 1919 | 100.00 | .... |
| 1909 | 100.00 | 121.23 | 1920 | 100.00 | .... |
| 1910 | 150.00 | 104.20 | 1921 | 100.00 | .... |
| 1911 | 300.00 | 218.38 | 1922 | 100.00 | .... |
| 1912 | 300.00 | 87.97 | 1923 | 100.00 | .... |
| 1913 | 300.00 | 42.98 | 1924 | 100.00 | .... |
| 1914 | 300.00 | 135.41 | 1925 | 100.00 | .... |
| 1915 | 100.00 | 61.14 | 1926 | 100.00 | .... |
| 1916 | 100.00 | 30.92 | 1927 | 50.00 | .... |
| 1917 | 100.00 | 32.53 | 1928 | 50.00 | .... |
| 1918 | 100.00 | .... | | | |

IN CONCLUSION.

It is very evident that the great accomplishments of the Committee fall in the first third of its history under the Chairmanship of Mr. Beringer and with the great incentive of the introduction of drug standards into the National Formulary.

The ideals of Dr. Beal, in his original address leading to the formation of the Committee, were apparently not a sufficient inducement to bring out the best and most strenuous efforts of capable men for the accomplishment of the great work that Dr. Beal set before the ASSOCIATION.

The work of the Committee under Chairman Beringer, comprising between 200 and 300 well-prepared monographs, was most remarkable. Not only was this work remarkable in *volume*, but the fact that most of it was *new* work and not merely a review of previously existing monographs, makes it even more striking.

It seems quite evident, then, from this history of the Committee, that some further inducement must be found to stimulate the members of the Committee to the accomplishment of the work that lies before them.

There are at least four other well-recognized agencies at work on standards for drugs and medicines; *viz.*, the U. S. P. Revision Committee, the N. F. Revision Committee, the Council on Pharmacy and Chemistry of the A. M. A. ("New and Non-Official Remedies") and the Association Official Agricultural Chemists whose standards partake of an official nature.

It is very certain that the A. PH. A. Committee on Standards of Drugs and Chemical Products cannot and does not wish to supplant any one of the standardizing bodies mentioned above. Is there an opportunity for this committee to serve pharmacy? Can we function to such purpose as will deserve recognition, and so as to be an incentive?

Your Chairman submits this report to the President of the ASSOCIATION, and the members of the Committee with the request that it be given careful study and that an early response be had from each recipient. Please do not neglect this report but send in an answer embodying your opinions as promptly as possible.

E. N. GATHERCOAL, *Chairman.*

Chicago, March 12, 1929.

(*To be continued*)

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# CORRESPONDENCE

## SOLUTION OF MAGNESIUM CITRATE.

It seems desirable to call your attention to a recent letter from the Food, Drug and Insecticide Administration concerning some of the Solution of Magnesium Citrate now offered to the pharmaceutical trade. If you will kindly help to give publicity to this situation many pharmacists will be on their guard against, and refuse to encourage, this dishonorable practice.

Dr. P. B. Dunbar, Assistant Chief writes:

> Our investigations of magnesium citrate solution have revealed that in a considerable number of instances manufacturers are supplying this article in packages containing less than 350 cc. (12 fluidounces). We find packages of $11^1/_2$ fluidounces, 11 fluidounces and even less on the market. The article, as you no doubt know, is highly competitive, so that the margin of profit is quite narrow. This no doubt is an incentive to reduce the volume contained in the individual bottles.
>
> The proviso in Section 7 of the Federal Food and Drugs Act would, of course, permit the manufacture and sale of magnesium citrate solution differing in quantity of contents as well as in other respects from the official standard for strength, quality and purity. It would be necessary only for the manufacturer to state upon the label in a plain and conspicuous manner that the article does not meet the Pharmacopœial requirements and to set forth the respects in which it differs from the official standard.

(Signed) E. FULLERTON COOK, *Chairman,*
Committee on Revision, U. S. Pharmacopœia X.

March 19, 1929.

# PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meetings of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

## CHICAGO.

The 181st meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held Tuesday evening, March 19th, at the University of Illinois School of Pharmacy.

The meeting was called to order by President Lindahl and the speaker of the evening, Dr. A. L. Tatum of the University of Wisconsin, was introduced. He gave an exceedingly interesting and instructive talk on "Drug Addiction and Its Physiological Basis."

Drug taking may result in the person becoming habituated to it but never becomes dependent on it. Addiction, on the other hand means that the person has severe suffering if without the drug and there is a physiological adaptation to the drug, in which the person is dependent on it.

It has been shown that a considerable tolerance to organic nitrates is developed, thus requiring more to produce the necessary effect. No tolerance is developed to inorganic nitrites.

In addiction the person requires less of the drug to produce the desired effect and becomes more sensitive to that drug. Opium and its derivatives produce addiction and also a tolerance.

Cathartics are habit forming, constipation being mainly due to bad dietetic and daily habits. Aspirin may create a habit with many, although it is merely masking the symptoms and not relieving the cause. Hypnotics such as the barbitals, chloral hydrate, etc., produce habits especially with nervous individuals, so that they think they need the drug in order to sleep. Such individuals become more sensitive to barbital compounds, and after continued use death may even be the result.

Alcohol and tobacco are psychic habits with no physiological involvements, although alcoholism may be classified as addiction. Cannabis, a depressant drug, presents an increasing danger, being used in cigaret form. The person is harmless but becomes a ready tool of someone else.

Cocaine, which is used by natives of South America, acts as a powerful stimulant and is not a narcotic. It stimulates the brain, producing exhilaration and diminishes all sense of fatigue. The victim learns to like it, he increases the dosage but reaches a place when he is afraid of a large dose. An increased sensitivity to cocaine develops and the dangers are thus greatly increased. It is a psychic effect as the person can be taken from cocaine without any physiological changes. The memory of the exhilarating effect brings them back to the use of cocaine.

A morphine addict has a desire to destroy the drug and then takes a larger dose to obtain the sedative effect to forget the desire. There are three theories regarding the action of morphine, one is that morphine becomes a necessity to all functions. In morphine poisoning most animals die in convulsions. On dogs, morphine in small doses is depressant and in large doses is a stimulant like strychnine. No tolerance develops in most animals to the stimulating action of morphine but there is a tolerance to the depressing action of morphine. Because

of the increased sensitivity to the stimulating action of morphine, the same dose may eventually cause death. A person may likewise be killed by a small depressing dose. There are three stages in the use of morphine, induction, tolerance and intolerance; in the latter stage the usual dose will not produce the accustomed depressing action.

Morphine stimulates certain parts of the central nervous system and depresses other parts. Repeated stimulation increases the irritability of the nervous system. The increased irritability decreases the amount of depression possible. For instance a small dose relieves pain, the person learns to like the sensation; repeated doses result in decreased amount of depression, the person becomes more nervous and requires a larger dose to quiet and finally no amount of morphine will give the depressing action. With increased irritability it is easy to throw the addict into convulsions. He is sick for the reason of the excess irritability and the inability to reach the normal depressant level. A cross tolerance to other depressants may also occur, that is, other similar drugs will fail to have any effect.

A general discussion followed during which the statement was made that atropine was not dependable as an antidote for morphine. Idiosyncrasy is a condition which cannot be satisfactorily explained.

Dr. Fantus paid high tribute to the work of Dr. Tatum on drug addiction but expressed his opinion that alcohol should be considered as producing addiction rather than habituation.

A rising vote of thanks was extended Dr. Tatum and the meeting adjourned.

S. W. MORRISON, *Secretary.*

## PHILADELPHIA.

The March meeting of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held Tuesday evening, March 12th, at the Philadelphia College of Pharmacy and Science. Preceding the meeting the annual dinner held in honor of the past-presidents of the Philadelphia Branch, was held in the College Building. About sixty members and guests were present.

President Adley B. Nichols opened the meeting with a few remarks on the significance of the annual dinner and meeting and expressed his appreciation to the past-presidents for their assistance and coöperation in making the Philadelphia Branch a successful organization.

Dr. William S. Wadsworth, Coroner's Physician, Philadelphia County, the speaker of the evening delivered an address on "Color." Dr. Wadsworth has devoted many years of his life to the study of this important subject. His personal experiences with outstanding scientists and the results of his many researches and investigations were related in the inimitable way so characteristic of him.

At the close of the address of the evening President Nichols called on the past-presidents then in the audience. The following responded, each giving intersting accounts of the activities and the work of the Branch during his term as President: Charles H. LaWall, Frank E. Stewart, W. L. Cliffe, Ambrose Hunsberger, W. W. McNeary, Ivor Griffith, B. C. Goodhart, J. W. England and J. W. E. Harrison. Past-presidents W. A. Pearson, E. F. Cook and Raymond Hendrickson who were present at the dinner were called away during the meeting.

The report of the committee on nominations was submitted and the election of officers resulted as follows:

*President*, Quintus Hoch.
*First Vice-President*, Louis Gershenfeld.
*Second Vice-President*, J. J. Kelly.
*Secretary-Treasurer*, Frank H. Eby.
*Delegate to the American Pharmaceutical Association*, Ambrose Hunsberger.

President Hoch took the chair and gave a brief address outlining the plans for the coming year. He expressed his appreciation to the members for having elected him to the office and promised a successful year.

A vote of thanks was extended to the retiring officers for their splendid work during the past year.

FRANK H. EBY, *Secretary.*

## NORTHERN OHIO.

The constitution and by-laws of Northern Ohio Branch are printed in this section. Several meetings of the Branch were held prior to those of November 9th and 16th, convened at the School of Pharmacy of Western Reserve University, a dinner preceded that of November 23rd. Dr. J. E. Tuckerman, Chairman of the Policy Committee of the Academy of Medicine, addressed the meeting on December 14th, at Hotel Statler, on "Organization." The meeting of January 11th also, was held at Hotel Statler. A dinner at Fenway Hotel preceded the meeting on February 8th; the business session following was convened in the main lecture room of Biology Hall, of the University;

the speaker of the evening was Dr. Louis Klein; his subject being "Newer Aspects of Gland Therapy." Members of the Cleveland Academy of Medicine attended the meeting.

The officers of the Northern Ohio Branch A. PH. A. are:

*President*, Edward Spease.

*Vice-President*, A. L. Flandermeyer.

*Secretary*, George Miller.

*Treasurer*, Paul Hudson.

*Council Members* for term ending December 31, 1929—Herbert Decker, Emil Petersilge; for term ending December 31, 1930—F. J. Bacon, F. J. Cermak, A. P. Gegenheimer, Alex Steiner; for term of 1931—H. E. Benfield, E. D. Davy, A. B. Ejbl, L. P. Miller; for term of 1932—A. L. Flandermeyer, George Miller, Paul Hudson, Edward Spease.

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## AMERICAN PHARMACEUTICAL ASSOCIATION BRANCHES.

Forms of Constitution and By-Laws of Local A. PH. A. Branches have heretofore been printed in these columns; the following presents a form applicable for A. PH. A. Branches, including student membership.

### CONSTITUTION AND BY-LAWS OF THE NORTHERN OHIO BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

#### PREAMBLE.

Recognizing the necessity for and the mutual benefits to be derived from a society devoted to professional and scientific pharmacy,

We, the undersigned, do agree to form such a society, and for its government do adopt the following Constitution and By-Laws:

#### ARTICLE I.—NAME AND OBJECTS.

*Section 1.* This society, a local branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, shall be known as the Northern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION.

*Section 2.* Its objects shall be as set forth in the preamble of this Constitution.

#### ARTICLE II.—MEMBERSHIP AND ELIGIBILITY.

*Section 1.* Any legally qualified reputable pharmacist or any other person interested in professional and scientific pharmacy, being a member in good standing in the AMERICAN PHARMACEUTICAL ASSOCIATION, shall be eligible for membership in the society.

*Section 2.* Each application for membership, except for Honorary membership, shall be signed by the applicant and endorsed by two voting members. Candidates for Honorary membership shall be proposed in writing by two voting members. Applications shall be submitted to the Council and notice thereof shall be given to all members of the society. At the next regular meeting of the Council votes shall be taken and a majority vote of the Council shall be required to elect an applicant to membership.

*Section 3.* The membership shall consist of six (6) classes as defined as follows:

(*a*) Active Member: A legally qualified reputable pharmacist resident in the district over which this branch is given jurisdiction by Chapter VII, Article 1, of the By-Laws of the AMERICAN PHARMACEUTICAL ASSOCIATION.

(*b*) Junior Member: A graduate in pharmacy who would otherwise be classed as active, but who has not in the opinion of Council, been in the practice of pharmacy for a period sufficient to establish himself; provided that in no case shall Junior membership be granted for a period longer than *three* years.

(*c*) Privileged Member: A graduate in pharmacy (1) who is not engaged in practice because of full-time research or teaching duties, or full-time public health work, or allied activities; or (2) who is not engaged in full-time practice because of disability or age.

(*d*) Associate Member: A physician, or a layman interested in sciences or professions allied to pharmacy, or a pharmacist, not a resident of this district, of good professional standing and a member of his local pharmaceutical association, if such an association exists.

(*e*) Honorary Member: A person whom the society deems worthy of special honor because of notable service to pharmacy.

(*f*) Student Member: Any student in pharmacy enrolled in and in good standing in his classes in a recognized school of pharmacy within this district. Student membership shall expire automatically upon graduation or in case of dismissal from college, when other membership may be granted at the discretion of Council.

*Section 4.* The Council shall have power to interpret Article II, Section 1, and the foregoing classification of members. It shall place members within the various classifications and may change members from one classification to another as conditions warrant.

*Section 5.* The resignation of members in good standing may be accepted and transfer to other local branches of the AMERICAN PHARMACEUTICAL ASSOCIATION may be granted by Council.

*Section 6.* Voting members may be transferred temporarily by Council to a non-active list because of disability. While so classified, they shall not pay dues.

*Section 7.* Council may at any meeting for causes set forth with specifications, consider the expulsion of a member and if it finds sufficient reason shall inform the accused that his resignation, if tendered, will be accepted. The accused shall be entitled upon demand to receive a copy of the charges against him. If the resignation shall not be tendered within one month after such notice is given, Council shall again consider the case and opportunity shall be given to the accused to be heard if he so desires. Council shall have authority to expel any member of the society for reasons which it deems sufficient, but the vote of two-thirds ($^2/_3$) of all the members of Council shall be necessary therefor.

### ARTICLE III.—PRIVILEGES OF MEMBERS.

All members shall be entitled to participate in the scientific deliberations of the society. The privilege of voting and holding office shall be restricted to Active, Privileged and Junior Members, these being referred to in this Constitution as Voting Members.

### ARTICLE IV.—OFFICERS AND COUNCIL.

*Section 1.* The management and control of the society shall be vested in a Board of sixteen (16) Trustees, which is also referred to in this Constitution as Council, members of which are elected as hereinafter provided. The routine business of the society shall be conducted by Council. Council shall consist of the President, Vice-President, Secretary and Treasurer and twelve (12) other members. The term of office of Councillors shall be four (4) years, or until their successors are elected and qualified. Four (4) Councillors shall be elected each year except that at the first election four (4) Councillors shall be elected for the term ending December 31, 1929, four (4) for the term ending December 31, 1930, four (4) for the term ending December 31, 1931 and four (4) for the term ending December 31, 1932. Vacancies occurring on the Board may be filled until the next annual election by the remaining members.

*Section 2.* Council shall render a monthly report to the society. A majority of the members of Council shall constitute a quorum.

*Section 3.* The officers of the society shall be a President, Vice-President, Secretary and Treasurer, all of whom shall hold office for one (1) year or until their successors are elected and qualified. The officers shall be elected by Council from among their own members by ballot vote. In 1929 and thereafter, no person shall be eligible for election as an officer until he has served at least one (1) year upon Council. The President and Vice-President shall not be eligible for immediate reëlection after serving a full year in office.

### ARTICLE V.—NOMINATION AND ELECTION OF COUNCILLORS.

*Section 1.* **Nomination.** A Nominating Committee of five (5) and a Tellers Committee of three (3) members shall be chosen by Council by ballot vote at its regular October meeting. At the regular November meeting of the society the Nominating Committee shall report at least two (2) eligible members for each vacancy upon Council. Additional names shall be placed on the official ballot upon written petition of twelve (12) voting members if submitted to the Nominating Committee within one (1) week following the regular November meeting of the society.

No names shall be placed upon the ballot until the Secretary has determined that the member is in good standing and is eligible and is willing to serve if elected.

*Section 2.* **Election.** Within ten (10) days following the regular November meeting of the society the Secretary shall mail to each voting member a ballot impressed with the seal of the society and addressed for return to the Tellers Committee. On it shall be printed the names of all members nominated in accordance with the preceding section and alphabetically arranged, together with instructions that one choice shall be indicated for each office to be filled and that ballots to be valid must be post marked not later than midnight of the Wednesday preceding the annual meeting of the society. The Tellers shall canvass the ballots on the day of the annual meeting of the society and report as duly elected those nominees receiving the greatest number of votes for the offices to which they were nominated, provided that any tie vote shall be decided by ballot of the members present at the annual meeting.

ARTICLE VI.—DUTIES OF OFFICERS.

*Section 1.* The President of the society shall be President of Council and a member *ex-officio* of all committees. In conjunction with the Secretary and Treasurer he shall sign all contracts authorized by Council and shall perform all the duties pertaining to this office and shall turn over to his successor all properties belonging to this office.

*Section 2.* The Vice-President, in the absence or disability of the President, shall perform all the duties of that office.

*Section 3.* The Secretary shall keep the minutes of all meetings of the society and of the Council and shall make and attest a proper record of the same. He shall collect dues, convey them to the Treasurer and perform such other duties as usually devolve upon a Secretary as directed by Council and turn over to his successor all records and properties belonging to this office.

*Section 4.* The Treasurer shall receive and have in charge all moneys belonging to the society and shall invest and disburse the same as may be ordered by Council. He shall keep an accurate account of moneys received and disbursed by him and shall perform such duties as usually pertain to the office of Treasurer and as may be directed by Council. He shall give bond for the proper performance of his duties in the amount required by Council, with a corporate surety approved by Council. The fee for this bond shall be authorized by Council and paid from the funds of the society. Upon the expiration of his term of office he shall turn over to his successor or to Council all money and property of the society in his hands.

*Section 5.* Council may employ an Executive Secretary and such other individuals as it may deem necessary and fix their compensation.

The duties of Executive Secretary shall be of an executive nature and all action by him shall be subject to the direction and approval of Council.

*Section 6.* The action of all of the aforesaid officers shall be subject to the approval of Council.

ARTICLE VII.—MEETINGS.

*Section 1.* The annual meeting of the society shall be held on the second (2nd) Friday of December in each year.

*Section 2.* The annual meeting of Council shall be held on the second (2nd) Friday of December in each year.

*Section 3.* Regular meetings of the society shall be held on the second (2nd) Friday of each month, except that meetings during the summer months may be omitted by order of Council provided the society holds not less than six (6) meetings in each year with an attendance of not less than nine members at each meeting, the proceedings of which have been transmitted to the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION for publication. Nine (9) Voting Members shall constitute a quorum.

*Section 4.* Regular meetings of Council shall be held on the second Friday of each month, except as it may recess during the summer months.

*Section 5.* Special meetings of the society may be called by the President at such time and place as Council may deem to be expedient and must be called by him on the written request of five (5) Voting Members of the society.

*Section 6.* Special meetings of Council may be called by the President at his discretion and must be called upon the written request of five (5) members of Council.

*Section 7.* Notices of special meetings of Council or of the society must be sent in written or printed form not later than three (3) days prior to the date of said meeting.

Special meetings of Council may be called by telephone provided each member of Council signifies consent to such meeting.

ARTICLE VIII.—COMMITTEES.

*Section 1.* Council shall have power to appoint such committees as it may find necessary to assist in the execution of its duties.

ARTICLE IX.—SECTIONS.

* * * * *

ARTICLE X.—DUES.

*Section 1.* The annual dues of the various classes of membership shall not exceed the following schedule:

| | | | |
|---|---|---|---|
| Active | $35.00 | Associate | $5.00 |
| Privileged | 15.00 | Student | 2.00 |
| Junior | 15.00 | Honorary | none |

*Section 2.* Power to place the dues at figures lower than the above schedule shall rest in the Council.

*Section 3.* The dues of all members, except Active Members, shall be due and payable within the first ten (10) days of each fiscal year. The dates of the fiscal year shall be set by Council.

*Section 4.* Dues of Active Members may be paid in installments as determined by Council.

*Section 5.* Any member in arrears for dues for three-quarters (3/4) of a year shall automatically be dropped from membership in the society. Such an individual shall not be eligible for reëlection until he has paid the dues in arrears at the date when he was dropped.

*Section 6.* The society shall remit annual dues to the AMERICAN PHARMACEUTICAL ASSOCIATION for all voting members who are not in arrears for current installment of dues or who are not on the non-active list.

ARTICLE XI.—AMENDMENTS.

Amendments to the Constitution may be made by assent thereto in writing by two-thirds (2/3) of the Voting Members of the society or by a vote of a majority of the Voting Members present at a meeting called for that purpose, two (2) weeks' notice of which shall have been given each Voting Member by mail.

ARTICLE XII.—ORDER OF BUSINESS.

*Section 1.* Annual Meeting of the Society.

1. Call to Order.
2. Reading of Minutes of Last Meeting.
3. Reports of Officers and Council.
4. Report of Tellers on Election of Councillors.
5. Miscellaneous Business.
6. Adjournment.

*Section 2.* Annual Meeting of Council.

1. Call to Order.
2. Election of Officers.
3. Miscellaneous Business.
4. Adjournment.

*Section 3.* All meetings of the society, the Council, the Committees and other sub-divisions shall be governed by Roberts' Rules of Order.

ARTICLE XIII.—SEAL.

The seal of the { society / corporation } shall be

## NORTHERN OHIO BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

### Classification Blank.

Name (in full).....Age.....
Home Address.....Tel.....
Business Address.....Tel.....
Class of Membership applied for.....

### Present Position.

Active Member:
Title or Position (Proprietor, Employee or Other Title).....Name of Firm.....
Junior Member:
Title or Position (Proprietor, Employee or Other Title).....Name of Firm.....
Privileged Member:
Title.....Name of Institution.....
Associate Member:
Position or Profession.....
Student Member:
Name of School.....Class.....

### Previous Experience.

Pharmacy School from Which Graduated.....
.....Year.....
Are You a Registered Pharmacist?.....
What States?.....Certificate Number....
Remarks: (Give any further information to support your claims for the desired classification).....
.....
.....

### To Be Filled Out by the Executive Office.

1. Date Received.....
2. Date Presented to Membership Committee.....
3. Recommendation of Committee.....
4. Recommendation Approved by Council....
.....Date.....
5. Date Filed.....

Remarks:

## APPLICATION FOR MEMBERSHIP.

To the Council of the Northern Ohio Branch of the American Pharmaceutical Association:

Gentlemen:

I desire to become a member* of the Northern Ohio Branch of the American Pharmaceutical Association.

.....(Name in Full)
(Date)..... .....(Business Address)
(Age)..... .....(Home Address)
Pharmacy School.....Year Graduated.....
Year Licensed in Ohio.....

The undersigned Voting Members take pleasure in endorsing the above application.

..... .....

* Classification will be determined by the Council.

I hereby declare that I approve of the Constitution and By-Laws of the Northern Ohio Branch of the American Pharmaceutical Association and that I will refrain from any and all illegal and unlawful acts in the practice of my profession or consider my membership in the Association forfeited. .....(Signature)

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## IMPROVEMENT OF GUTZEIT AND MARSH TESTS FOR ARSENIC.*

Research work, upon which I have been engaged in the research laboratory of the College of Pharmacy of the University of Minnesota since last fall, looking toward the improvement of the well-known Gutzeit's and Marsh's tests for arsenic by the use of a catalyst and the substitution of aluminum for zinc as a means of liberating hydrogen, has shown that aluminum can be used with advantage in the place of zinc. So far better and more uniform arsenic stains and deposits have been obtained by the use of aluminum as against zinc. The addition of stannous chloride to the aluminum-acid reaction mixture is necessary as it stimulates the evolution of hydrogen and serves to displace the last traces of arsenic present.

"Complete test procedures will be presented at a later date."

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* A preliminary report by L. P. Mayrand, candidate for Master's Degree in Pharmacy, University of Minnesota, Minneapolis, Minn.

# ASSOCIATION BUSINESS

## AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1928-1929.

Office of the Secretary, 10 West Chase Street, Baltimore, Md.

LETTER NO. 6.

February 8, 1929.

*To the Members of the Council:*

59. *Election of an Architect for the Headquarters Building.* The following communication has been received from Chairman Dunning:

"Recently I communicated to the Committee on Plans my belief that the time had now arrived when the Committee should recommend an architect for the Headquarters Building to the Council for election. This suggestion was made because we now have in bank approximately enough money to erect a building on our site in Washington of the capacity tentatively discussed by the Committee on Plans sometime ago. At that time it was the general estimate that a buiding 140 feet long by 50 feet wide, two stories and basement, would be sufficient for the needs of the ASSOCIATION, and this estimate was only to arrive at some idea of the space required.

"Previous to this suggestion to the Committee, I investigated the proposal to select an architect by the competitive plan and did not find this plan acceptable because it is more expensive and because, under the rules governing such contests, we are required to accept the plan approved by the judges. The position and surroundings of our site practically determine the style of architecture we must and should follow in order to secure the approval and coöperation of the Commission of Fine Arts, both of which it is necessary to have.

"It was my conclusion that we should select a nationally known architect acquainted with the plans for the development of that section of Washington and who would be acceptable to the Fine Arts Commission and other governmental agencies, the guidance and advice of which will be of great assistance to us in working out our problem satisfactorily. In accordance with these conclusions I made some inquiries which lead me to believe that John Russell Pope of New York was an acceptable architect from all points of view and especially on account of his participation in and close contact with the development of the section of Washington in which our site is located. Mr. Pope was for some time a member of the Fine Arts Commission and is now the architect of the Roosevelt Memorial. I am pleased to advise that the Committee on Plans unanimously approves the selection of Mr. Pope and recommends to the Council his selection as architect of the Headquarters Building.

"Several conferences have been held with representatives of Mr. Pope's office during which our proposal has been exhaustively considered, and Mr. Pope and those associated with him have expressed enthusiastic interest in working out our problem to the best advantage. The following letter outlines the arrangement which Mr. Pope suggested and under which he will undertake to design our building and supervise its erection:

New York, January 11, 1929.

Dr. H. A. B. DUNNING
Baltimore, Md.

Re: American Pharmaceutical Bldg.

Dear Doctor Dunning:

In our conference at Baltimore, we suggested it might be helpful to your position in this contemplated work if we outlined information regarding our rates and procedure. We trust the following will be satisfactory to you. If not, we would be glad to have your reaction.

Our rate will be the standard minimum, namely, 6% on the cost and we conduct our work in accordance with the standard practice of the American Institute of Architects. In order to be helpful, we will agree at the very first stage to furnish you with a diagrammatic plan and elevation in rough form and without giving serious consideration to a final arrangement, but sufficient to indicate with substantial correctness, the cubage involved in the proposed building and to give you a comprehensive idea of a

plan and the general character of a building. We made a point of this at our conference as important to your interest, stating that it was our desire to avoid any unnecessary architectural work and expense in connection with the development of the project. In the event that the work should stop at this stage, we would be very glad to accept an arrangement whereby we shall be compensated only for the actual cost of our services.

The rough scheme is generally satisfactory and when you authorize us to proceed further in the completion of the preliminary studies, etc., we will then charge in accordance with the schedule of proper minimum charges of the American Institute of Architects, Article No. 9. At this time we will then prepare a contract between your association and our office.

In the meantime, I think the above understanding will be sufficient. As we get into the problem we gain momentum in our enthusiasm. Mr. Pope expects to write you in a few days telling you how pleased he is with this opportunity.

Yours very truly,
OFFICE OF JOHN RUSSEL POPE
(Signed) D. P. HIGGINS.

"During the discussion with Mr. Pope, the ASSOCIATION received an invitation from the Fine Arts Commission to discuss our project with them. Secretary Kelly and I met with the Fine Arts Commission on January 22nd and had a most satisfactory interview with them, as a result of which the Fine Arts Commission is coöperating with us wholeheartedly. As the situation now stands we have the sympathetic interest of the Fine Arts Commission and of the Parks and Planning Commission, and their help will be of the greatest value to us.

"At our suggestion Mr. Pope's office sent two representatives with us to the meeting with the Fine Arts Commission, at which time Mr. Pope submitted a tentative design for our building which was found to conform with the ideals of the Commission and which the Commission approved. This tentative plan is being completed by Mr. Pope in accordance with the arrangement outlined above and will be submitted to the Committee on Plans within a short time for study.

"It will be noted that Mr. Pope's charges are the standard minimum and that his work is conducted in accordance with the standard practice of the American Institute of Architects.

"It was my intention to bring up the selection of an architect prior to any contact with the Fine Arts Commission but when the invitation from this body was received we felt it necessary to comply with it for obvious reasons.

"In turn this development makes it desirable to select an architect promptly and for this reason I am asking the Council to act on this recommendation of the Committee on Plans at the earliest possible date."

(*Motion No. 21*) *It is moved by Dunning that John Russel Pope be elected as architect for the Headquarters Building and that the President, Secretary and Treasurer of the Association be authorized to enter into a contract with Mr. Pope in accordance with the agreement stated in the letter addressed to H. A. B. Dunning by the Office of John Russel Pope under date of January 11, 1929 and signed by D. P. Higgins.*

By direction of the Chairman of the Council a vote on this motion is called for at this time.

E. F. KELLY, *Secretary.*

## LETTER NO. 7.

March 19, 1929.

*To the Members of the Council:*

*60. Year Books, Volume 16 (for 1927) and Volume 17 (for 1928). Motions No. 17 and No. 18* (See Council Letter No. 5, page 183) have been carried and the Report of the Progress of Pharmacy for 1927 and that for 1928, with the usual ASSOCIATION data, will be printed in one volume, the contract for which has been awarded to the Lord Baltimore Press, Baltimore, Md.

*61. Election of Members. Motions Nos. 19 and 20* (See Council Letter No. 5, page 187) have been carried and applicants for membership numbered 98 to 115 inclusive, and applicants for membership numbered H-11 to H-54 inclusive are delcared elected.

*62. Election of an Architect for the Headquarters Building. Motion No. 21* (See Council Letter No. 6, preceding) has been carried and Mr. John Russell Pope is being notified of his election. The President, Secretary and Treasurer of the ASSOCIATION will enter into a contract with Mr. Pope in accordance with the agreement set out in Council Letter No. 6.

*63. Life Membership.* In accordance with Article IV of Chapter IX of the By-Laws, Ethan Allen Burford, Honolulu, T. H. has become a life member through the payment of $100.00; Lawrence Edward Highley, Hot

Springs, S. Dak., through the payment of $50.00; Maximilian Wilmer Friedenburg, Long Beach, Calif., through the payment of $25.00; Mrs. Bertha L. Peacock, Philadelphia, Pa., through the payment of $15.00; and the following have become life members through the payment of dues for thirty-seven consecutive years: Franklin Samuel Hereth, San Francisco, Calif.; Eugene Reinhold Selzer, Cleveland Heights, Ohio; Frederick John Wulling, Minneapolis, Minn. and Lauriston Stephen Smith, Santa Monica, Cal.

Life Membership certificates are being issued to those members.

*64. Applicants for Membership.* The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 116, S. J. Blackstone, 203 Johnson Ave., Newark, N. J.; No. 117, Monroe Franklin Brown, 874, Union Ave., Memphis, Tenn.; No. 118, Fred'k S. Burnham, 430 Lexington St., Auburndale, Mass.; No. 119, Joseph J. Burniac, 7800 Michigan, Ave., Detroit, Mich.; No. 120, R. C. Byce, 528 Alber Ave., East Lansing, Mich.; No. 121, Alfredo Moscardo Climent, Salvador 17, Valencia, Spain; No. 122, Henry Colle, 410 Pine St., Maryville, Calif.; No. 123, Herbert W. Decker, 12467 Cedar Road 1, Cleveland, Ohio; No. 124, Charles LeRoy Doherty, 621 Main St., Rapid City, S. Dak.; No. 125, Benjamin Fyne, 1500 So. 8th St., Philadelphia, Pa.; No. 126, Harry Goldschmidt, 134 First Ave., New York, N. Y.; No. 127, Herbert Nathan Goldstone, 1216 E. Baltimore St., Baltimore, Md.; No. 128, Emil Hargens, Hot Springs, S. Dak.; No. 129, Joseph B. Hawkins, 2722 W. Farragut Ave., Chicago, Ill.; No. 130, John Lyndale Herchmer, 12 14th Ave., S. E., Aberdeen, S. D.; No. 131, Leslie O. Hill, c/o The W. T. Rauleigh Co., Freeport, Ill.; No. 132, Morris J. Jones, Bowdle, S. Dak.; No. 133, Victor E. Jones, Clark, S. Dak.; No. 134, Max Kritt, 6140 Hazlett Ave., Detroit, Mich.; No. 135, Ruben G. Krohn, 321 Wisconsin Ave., Madison, Wis.; No. 136, Frederick Dudley Lascoff, 1223 Lexington Ave., New York, N. Y.; No. 137, Henry Lutzenkirchen, 32 W. Randolph St., Chicago, Ill.; No. 138, Lewis Elbert Martin, 715 S. Wood St., Chicago, Ill.; No. 139, J. J. McKay, 332 Pierre St., Pierre, S. Dak.; No. 140, Louis V. Merz, 59 W. Austin Ave., Chicago, Ill.; No. 141, Richard H. Ottman, Rapid City, S. Dak.; No. 142, Hubert Fred Owens, 2335 Addison St., Chicago, Ill.; No. 143, Ellsworth O. Prather, Jr., 874 Union St., Memphis, Tenn.; No. 144, William Rabinowitch, 1440 Broadway, New York, N. Y.; No. 145, R. J. Schiffmann, 1734, N. Maine St., Los Angeles, Calif.; No. 146, Wm. L. Schrader, 141 W. Austin St., Chicago, Ill.; No. 147, John Wm. Smith, 420 South 6th St., Minneapolis, Minn.; No. 148, John James Spranza, 5548 W. Congress St., Chicago, Ill.; No. 149, W. W. Stroop, 5202 Cates Ave., St. Louis, Mo.; No. 150, Albert Speidel, 70 Ship St., Providence, R. I.; No. 151, David Svigals, 29 Linda Ave., White Plains, N. Y.; No. 152, George Washington Taylor, 912 Elizabeth St., Waycross, Ga.; No. 153, Harold O. Trotter, 267 Berkley Rd., Indianapolis, Ind.; No. 154, Albert K. Wampole, c/o The Henry S. Wampole Co., Baltimore, Md.; No. 155, Charles E. West, 338 Berry St., Brooklyn, N. Y.; No. 156, Raymond D. Wisler, 3809 N. Cicero Ave., Chicago, Ill.; No. 157, Frank Zimmermann, 4126 N. Lawler Ave., Chicago, Ill.

*(Motion No. 22) Vote on applications for active membership in the American Pharmaceutical Association.*

*65. Applicants for Membership on Account of Contributions to the Headquarters Building Fund.* The following non-members of the A. Ph. A. have pledged $25.00 or more to the Headquarters Building Fund and have made a cash payment of $5.00 or more. They are entitled to membership.

H-55, Alfred R. Bigot, 501 Howard St., Hibbing, Minn.; H-56, Isidore Bloch, 2704 University Ave., New York, N. Y.; H-57, Bernard Joseph Bush, 1238 3rd Ave., San Francisco, Calif.; H-58, George Connolly, 2149 Westchester Ave., New York, N. Y.; H-59, Harry Cooper, 1561 Sterling Place, Brooklyn, N. Y.; H-60, Maurice Ambrose Drain, 409 Dubois St., Vincennes, Ind.; H-61, Alexander Paul Deckman, 171 Remington St., Bridgeport, Conn.; H-62, William Ellsworth Dudley, 131 Cushing Ave., Dorchester, Mass.; H-63, Lawrence Beverly Dunn, 2620 Anza St., San Francisco, Cal.; H-64, Harry J. Fine, 1422 S. Kolin Ave., Chicago, Ill.; H-65, Horace J. Ford, Joelton, Tenn.; H-66, Wellford Minson Frayser, 1603 Oakwood Ave., Richmond, Va.; H-67, R. Franklin Hart, Jr., c/o Kelso Drug Co., Kelso, Wash.; H-68, Albert Alexander Hyde, 1400 E. Douglas Ave., Wichita, Kans.; H-69, Dominich Joseph Lofrumento, 1143 Castle Hill Ave., Bronx, N. Y.; H-70, Nathan Calmin Margulies, 781 Multnomah St., Portland, Oreg.; H-71, Matthew Warren

Miller, 884 Riverside Drive, New York, N. Y.; H-72, Barney Mollov, 1830 Arthur Ave., New York, N. Y.; H-73, Albert B. Morgan, 169 Pleasant St., Malden, Mass.; H-74, Muriel Ursula Oertling, 7315 Frereb St., New Orleans, La.; H-75, Jules Scribner Pernot, Jr., 514 E. 23rd St., Paterson, N. J.; H-76, Julian Merwin Wells, 107 Belvedere St., San Francisco, Cal.; H-77, Chingyin Dorothy Wen, Loma Linda, Cal.; H-78, LeRoy Joseph Wenzel, 526 Mountain St., Pittsburgh, Pa.; H-79, Robert Haws Wuensch, 30 South Kingman Road, South Orange, N. J.

(*Motion No. 23*) *Vote on applications of contributors to the Headquarters Building Fund for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

## SOCIETIES AND COLLEGES.

FROM SOUTH DAKOTA PUBLICITY COMMITTEE BULLETIN NO. 2.*

On August twenty-sixth, the seventy-seventh Annual Convention of the AMERICAN PHARMACEUTICAL ASSOCIATION will open in the Alex Johnson Hotel, at Rapid City, South Dakota.

On that day, and the busy week following, members in attendance will become conscious of having been surrounded by a new atmosphere—that of the West. Atmosphere which embodies the balsamic tone of the air from the age-old Hills in the background, and that indefinable breath of the Old West, whose spirit has been so ably recorded by Badger Clark, the Cowboy Poet of the Black Hills—a spirit which has been caught up by the succeeding generations, who have carried on those basic traditions and woven them into the fabric of modern progress.

About the time the AMERICAN PHARMACEUTICAL ASSOCIATION was being organized, seventy-seven years ago, the Black Hills were being looked upon by the speculative eye of the fur trader and prospector. When the ASSOCIATION was celebrating its first quarter-century milestone, and beginning to taste the fruits of its toils, men had discovered the mineral wealth of the Hills. The Hills, through the hectic days that followed, reached a plane of organization and systematic advancement by struggle and a survival of the fittest, and the utilization of the bounteous resources hidden in them by nature ages ago. The ASSOCIATION, through the same period, quietly and systematically forged stronger links into the chain of progressive Pharmacy from the ideals laid down throughout centuries untold.

The ASSOCIATION will meet at Rapid City to take up and pass upon the serious phases of pharmacy to-day. The purpose, progress and preservation of professional pharmacy are guarded and upheld by the ASSOCIATION as by no other organization.

For moments of relaxation, or for a few days of outing, following the convention, the Black Hills afford an opportunity rivaled by no other spot of equal area in the world.

It is a place of enthralling beauty. The scenery is unique, richly varied, pleasingly harmonious and impressively magnificent. The granite mountains are rugged, picturesque, inspiring and easily accessible. Splendid new highways, marvels of engineering skill, ribbon the rugged slopes and take one at once into the heart of the most interesting and spectacular areas of this fairy-land. Here, close at hand, one may study to his heart's content the makeup of mountain, park and valley, the peculiarities of topography, the courses of the swift-flowing streams, the coloring of the many kinds of rocks, the great variety of interesting minerals and the unending array of plant and animal life native to the region. Of rainfall there is just enough, and the rollicking, trout-laden streams, crystal clear, tumble merrily down their sharply chiseled valleys, and carry gladness to many a charming nook.

Plan now to attend the Rapid City meeting, August 26th–31st. Railroad rates are assured from every point in the United States, and the best of graveled highways make the Hills accessible from every direction.

Rapid City—the Gateway to the Black Hills—at once the result and exemplification of the transformation from the Old West to the New—so ably caught by the Black Hills' Poet, Badger Clark:

"They build high towns on their old log sills,
Where the great, slow rivers gleamed,
But with new, live rock from the savage hills
I'll build as they only dreamed.
The smoke scarce dies where the trail camp lies,
Till the rails glint down the pass;

*AMERICAN PHARMACEUTICAL ASSOCIATION to meet in the "Wonderland of America."

The desert springs into fruit and wheat,
And I lay the stones of a solid street
Over yesterday's untrod grass."

Reports from Winnipeg indicate that a large number of Canadian druggists intend to avail themselves of the nearness of the A. PH. A. Convention this year. Plans are under way for making up a motor caravan, to start at Winnipeg and reach Rapid City just before the convention.

## SECTION ON EDUCATION AND LEGISLATION.

*Call for Papers.*

The program of the Section on Education and Legislation is now in course of preparation. As secretary of the section, I desire to secure a number of interesting constructive papers which fall within either phase of the section's scope for our next meeting. Will you prepare such a paper for presentation before our group when it meets at Rapid City in August?

No other period in the history of pharmacy has given rise to so many vital problems pertaining to education and legislation. You can contribute to the solution of these problems by presenting your ideas before this section.

There is no fixed limit on the length of papers. However, experience has proven that papers condensed so that they require no more than ten or fifteen minutes for presentation are most desirable, give ample time to set forth ideas in a concise manner, and permit full discussion.

Please inform me at once of the title of the paper which you will contribute. You may prepare the paper at your convenience but send in the title at once.

Anticipating early assurance that you will present a paper before this section at Rapid City in August, I remain

(Signed) GLENN L. JENKINS, *Secretary.*

*For officers of the Sections see page X, Advertising Section or March Jour. A. Ph. A., pages 309–310.*

## AMERICAN MANUFACTURERS OF TOILET ARTICLES.

A very successful annual meeting was held by the American Manufacturers of Toilet Articles, April 2nd–4th, at Hotel Biltmore, New York City. The address of President John A. Handy was comprehensive. He recommended some changes in the by-laws which included a provision for the publication of monographs on raw materials and compilation of drugs, etc., entering into the preparation of perfumes and other toilet articles. The Association also went on record favoring the Capper-Kelly Price-Maintenance Bill, disapproving the transfer of the Prohibition Bureau from the Treasury Department to the Department of Justice. The work of the Prohibition Commissioner was commended.

President Handy expressed his thanks to the members of the Entertainment Committee and his appreciation of the beautiful brochure prepared by Richard LeGallienne on "The Romance of Perfume."

Dr. Curt P. Wimmer added to the program by an address on "Possible Uses of Ultraviolet Radiations in the Essential Oil Industry."

The following officers were elected for the ensuing year:

*President*, John A. Handy; *First Vice-President*, H. H. Bertram; *Second Vice-President*, E. B. Hurlbutt; *Secretary-Treasurer*, Daniel J. Mulster.

## THE BRITISH PHARMACEUTICAL CONFERENCE.

This year's British Pharmaceutical Conference will be held in Dublin, June 24th–28th, after an interval of twenty-eight years. It is said that 582 reservations have so far been made for the convention, and the meeting promises to be largely attended.

## THE SOCIETY FOR THE HISTORY OF PHARMACY.

The Society for the History of Pharmacy will be held in Berlin, Germany, May 2nd–5th. An extensive program has been prepared.

## A PHARMACEUTICAL CORPS IN THE BRITISH ARMY SERVICE AND IN THE U. S. ARMY.

*The Pharmaceutical Journal and Pharmacist* of March 23rd, has a comprehensive editorial on "A Proposed Army Pharmaceutical Service for the United States." The editorial gives an account of the hearing on the Bill before the House Committee on Military Affairs, and concludes with a comparison of that submitted to Congress with the scheme for a British Army Pharmaceutical Service as propounded by Surgeon-General Evatt in 1906, and on more systematic lines by President E. Saville Peck. We quote:

"The fundamental principle common to the American and British projects is that they should be an organized and permanent Army Pharmaceutical Service with a staff of com-

missioned pharmacist officers, similar to the establishment of this kind in Continental armies. The League of Ex-Service Pharmacists have by intensive effort secured a large measure of support from members of Parliament for this demand, and will have a valuable opportunity to press their case on Parliamentary candidates at the forthcoming General Election. In this country, in the light of the admissions made by the War Office in the course of the inquiry and negotiations by the Joint Committee of representatives of that Department and of the Pharmaceutical Society, there ought to be no need for special legislation to create an Army Pharmaceutical Service. But if the War Office remains adamantine in its refusal to adopt this reform it will become the duty of the pharmacist members whom we hope to see in the new House of Commons to take the matter in hand and do their utmost to bring about the abolition of this scandalous anachronism."

## D. R. B. BULLETIN NO. 6.

D. R. B. No. 6 summarizes the results of the Nationwide survey of Toilet Goods Stocks in Retail Drug Stores.

Several thousand pharmacists participated in this research. All types of drug stores and all parts of the country are represented.

This report is of intense value to every retail druggist who will study it and apply in his own store the facts and principles laid down in its pages. This Bulletin should be studied with Bulletins 5A, 5B, and 5D.

D. R. B. Bulletin 5-C, to be mailed, gives toilet goods facts about a city cut-rate drug store. 5-D, will give toilet goods facts about a country drug store. The principles set forth in these bulletins apply with equal force to all drug store merchandise.

*See your wholesale druggist or write for the Bulletins to Secretary E. L. Newcomb, 51 Maiden Lane, New York City.*

## APRIL AND MAY ASSOCIATION MEETINGS.

The Golden Jubilee meeting of Kansas Pharmaceutical Association will be held at Jayhawk Hotel April 15th–18th, in Topeka. California and Oklahoma meet in May; the latter in Oklahoma City, May 14th–16th, and the former in Eureka, May 27th–29th.

The American Drug Manufacturers' Association meets in Grove Park Inn, Asheville, May 2nd–7th. The Sales and Advertising Committee has prepared a program for May 6th, at which time there will be discussions on the following subjects:

"Does Pharmaceutical Advertising in Drug Journals Pay?" Donald Merrell; "Does Pharmaceutical Advertising in Medical Journals Pay?" Fred A. Lawson; "Does Sales Research Pay?" Frank B. Kirby, M.D.; "Costs, Customers and Profits," H. C. Dunn; "How Can We Asist the Retailers?" Turner Currens; "How Can We Coördinate Sales and Advertising?" R. D. Keim; "How Do We Know Detailing Pays?" R. M. Cain; "Do Exhibits Pay?" Harry C. Phibbs.

## BALTIMORE RETAIL DRUGGISTS' ANNUAL MEETING.

The 13th annual meeting of the Baltimore Retail Druggists' Association proved a great success. The program was well arranged and carried through without a hitch by President Harris and his Committees. Among the Speakers were Mayor William F. Broening, former U. S. Attorney Hon. Robert R. Carman, and R. E. Lee Williamson, former president of the B. R. D. A. Among other guests, were the following:

President Walter Morgan, of the Delaware Pharmaceutical Society; President Paul Pearson, of the District of Columbia Retail Druggists' Association; A. L. Sullivan, Maryland Food and Drug Commissioner; President Howell W. Allen, of the Maryland Pharmaceutical Association; E. C. Brokmeyer, General Counsel N. A. R. D.; Dr. Robert H. Riley, Director of Health of Maryland; Editor E. G. Eberle, of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION; Dr. A. G. DuMez, Dean of the College of Pharmacy of the University of Maryland; Secretary Robert L. Swain, of the Maryland Board of Pharmacy; Secretary E. F. Kelly, of the AMERICAN PHARMACEUTICAL ASSOCIATION; Hon. Howard Bryant, President of the City Council of Baltimore.

The banquet committee consisted of: M. Strasburger, Chairman; P. J. Boenning, Charles L. Meyer, Wm. G Lauer, S. Y. Harris, G. P. Hetz, Wm. H. Pensel.

The officers of the association are:

*President*, Samuel Y. Harris; *Secretary*, M. Strasburger; *Recording Secretary*, W. H. Kratz; *Treasurer*, P. J. Boenning; *First Vice-President*, W. G. Lauer; *Second Vice-President*, L. S. Williams; *Third Vice-President*, George P. Grau; *Fourth Vice-President*, L. G. Munzert.

Among the Washington visitors were: Samuel L. Hilton, E. C. Brokmeyer, Paul Pearson, A. F. Gorsuch. Walter Morgan, Tom Smith and Larry Sanders made up the delegation from Delaware.

## CHAIRMAN J. LEON LASCOFF HONORED AND THE COMPLETION OF THE PHARMACEUTICAL RECIPE BOOK CELEBRATED.

More than four hundred guests were present at Hotel Pennsylvania, March 18th, to honor Chairman J. Leon Lascoff, of the Committee on A. PH. A. Recipe Book and to celebrate the completion of this work. The occasion was arranged by New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION. Robert S. Lehman, Chairman of the Dinner Committee presided and H. V. Arny did the honors as toastmaster. The speakers were: Dean William C. Anderson, Dr. Walter Bastedo, Dr. George C. Diekman, Jonah J. Goldstein, Nathaniel Nicolai, Secretary E. F. Kelly, Dr. Augustus S. Downing, President H. A. B. Dunning and representatives of various organizations.

President Hugo H. Schaefer presented the second copy of the Recipe Book to Chairman Lascoff. Robert S. Lehman, on behalf of the New York Branch A. PH. A. presented a testimonial in the form of a diploma. Various organizations did likewise and added honorary membership to their expressions of esteem. Mrs. Lascoff was favored with a large bouquet of beautiful flowers. After responding to the compliments paid him Chairman Lascoff gave a brief summary of his activities and presented Editor Griffith with a copy of the Recipe Book and President Dunning, of the A. PH. A., with the original manuscripts which formed part of the basis of the book.

References to the celebration and the Committee having the preparation of the Book in charge were made in the March number of the JOURNAL.

## BACTERIOLOGY EXHIBIT AT THE SCHOOL OF PHARMACY, UNIVERSITY OF ILLINOIS.*

The second annual bacteriological exhibit was held at the University of Illinois, School of Pharmacy, on January 24 and 25, 1929. The exhibit consisted of work done during the semester, by students of the Senior class and there was also a display of stock cultures.

The work in bacteriology consists of the isolation and identification of an unknown organism, the preparation of forty-five to fifty known cultures of pathogenic, non-pathogenic, chromogenic and anaerobic bacteria, as well as yeasts and molds, the student preparing his own culture media throughout the course.

The exhibit consisted of the work selected by the teachers, as well as specially arranged displays. Characteristic tube cultures, neatly sealed and labelled together with notes and drawings were prominently displayed.

Phenol coefficients of several well-advertised germicides were worked out as accurately as possible. Air counts were obtained from several sections of the city, at various altitudes, in crowded public places, in vacant places, in occupied school rooms, in vacant rooms, basements, etc. It was interesting to see the comparison between the crowded places and unoccupied ones, high altitudes, etc.

Milk counts on samples obtained from the city's best known dairies—pasteurized, certified, buttermilk, sour milk, etc. Water counts on samples obtained from many of the well-advertised mineral waters, tap water, spring water, cathartic water, distilled water, river water, beverages, etc., were made and compared. Twelve to fourteen members of the colon-typhoid group were studied as to their reactions in various media.

The entire exhibit was arranged well, placards accompanied the displays so that one who had never studied the subject could obtain some idea of the work done and its value to the student.

Students and faculty in the school were invited, the city journals carried an announcement inviting any one interested to attend. There was a nice attendance and the visitors seemed to enjoy the various displays.

* From a report by Esther Meyer, of Department of Bacteriology.

## UNIVERSITY OF MICHIGAN, COLLEGE OF PHARMACY.

The College of Pharmacy of the University of Michigan wishes to acknowledge its indebtedness to several Michigan pharmaceutical manufacturers as well as to the Michigan State Pharmaceutical Association for the generous way in which they have supported research work in synthetic drugs. E. S. Blake, the recipient of the Frederick Stearns and Company Fellowship, is preparing a series of local anæsthetics. F. D. Smith, Parke, Davis

& Company Fellow, is investigating a number of organic arsenicals. O. J. Weinkauff, Upjohn and Company Fellow, is occupied with a problem on synthetic laxatives; J. L. Powers is studying a number of new pyrrole derivatives and U. O. Oakdale is synthesizing a variety of new organic derivatives of antimony and bismuth.

THE NEW MEXICO STATE BOARD OF PHARMACY AND STATE ASSOCIATION.

Secretary, David L. C. Hover announces that the Spring Meeting of the New Mexico State Board of Pharmacy and examination of candidates will be held in the Franciscan Hotel, Albuquerque, May 20th at 9 A.M.

During the same days there will be a meeting of the State Pharmaceutical Association.

BROOKLYN COLLEGE OF PHARMACY.

Ground was broken on March 12th for the new building of the Brooklyn College of Pharmacy of Long Island University. The ceremonies were attended by members of the student body, the faculty and of the King's County Pharmaceutical Society. It is expected that the building will be ready for occupancy for the opening session of the school in September.

OFFICERS OF ALUMNI ASSOCIATION, ST. LOUIS COLLEGE OF PHARMACY.

The Alumni Association of the St. Louis College of Pharmacy elected Wm. C. Bolm, *President;* C. H. Winkelmann, *First Vice-President;* W. D. Martin, *Second Vice-President;* Prof. W. C. Clark, *Secretary;* Charles Gietner, *Treasurer;* and Dr. W. D. Aufderheide, *Registrar.* Mr. Gietner is now serving his fiftieth year as Treasurer.

## PERSONAL AND NEWS ITEMS.

W. H. Whisenant, Chairman of the Texas Legislative Committee, reports on the new pharmacy law in the *Southern Pharmaceutical Journal* and *Texas Druggist.*

**President C. P. Wimmer** announces that those desiring information on the European Tour, under the auspices of the New York German Apothecary's Society, should address him at 115 West 68th St. The party sails June 27th.

Speakers at the Northestern Branch meeting, held jointly with the Wulling Club, March 5th, were: **E. Sater, Richard Laska, Rugnar Almin, L. P. Mayrand** and **Dean Wulling.** The meeting was in the nature of a symposium on "The Aims and Objects of Pharmaceutical Practice of To-Day." About 200 were present.

**Dean Charles E. Caspari** was given a dinner, on April 4th, by his friends and associates, commemorating the 25th anniversary of his becoming a member of the faculty of St. Louis College of Pharmacy. The messages, large attendance and the remarks of the speakers evidenced the high regard and esteem in which the Dean is held in St. Louis and by American pharmacists throughout the country.

At the graduation exercises of the Yeshiva College, New York, held in its new buildings, Amsterdam Avenue and 186th Street on April 2nd, the degree of Doctor of Literature was bestowed upon **Dr. David I. Macht,** Lecturer in Pharmacology, Johns Hopkins University, and Director of the Pharmacological Laboratory, Hynson, Westcott and Dunning, in recognition of his scientific investigations concerning the materia medica, pharmacology and hygiene of the ancient Hebrews.

**President Denny Brann,** N. A. R. D., was the principal speaker at a joint luncheon meeting of the Minneapolis Veteran Druggists' Association and the Retail Druggists' Association. Mr. Brann is *Vice-Chairman* of the Section on Commercial Interests, A. PH. A.

**Dean F. W. Nish,** of the California College of Pharmacy, has been ill for several weeks, but has returned to his duties.

**Dr. John C. Krantz, Jr.,** has perfected the manufacture of sodium malate, a substitute salt for those who cannot use sodium chloride. Dr. Krantz was the speaker at the Men's Club, of the Church of St. Michael and All Angels, April 8th, on "Chemistry in the Crises of Health." His activities in pharmaceutical research and in the AMERICAN PHARMACEUTICAL ASSOCIATION are well and favorably known.

**Secretary W. Bruce Philip,** in his *Weekly Information Letter,* is cautioning pharmacists to bottle **Spirit of Ethyl Nitrite** in accordance with pharmacopœial suggestions, and also advises them to keep a record of purchases of pharmaceuticals, so that the source may be referred to, should it become necessary.

A recent report in the *New Jersey Pharmaceutical Journal,* by Secretary Robert P. Fischelis is pleasing, because of the small percentages of deficiencies in strength of preparations examined. The official drug report of the Bureau of Foods and Drugs of

the Maryland State Department of Health for January and February, published in the *Maryland Pharmacist*, by Dr. R. L. Swain, for March is, at least, equally pleasing. Such reports reflect credit and show that pharmacists are mindful of their responsibilities and also emphasizes the importance of pharmacy; for, deficiency in strength may be as serious a factor in the outcome of sickness as an overdose.

Edward T. Clark, of Northampton, Mass., for the past eight years personal secretary of President Coolidge, is now active Vice-President of Drug, Inc.

**Edward V. Sheely,** prominent pharmacist of Memphis, Tenn., has been appointed Postmaster of Memphis; the appointment has been approved.

**B. A. Deterling** has completed his third term as Mayor of Granite Falls, Minn.

Dr. P. J. Hanzlik, professor of pharmacology, Stanford University School of Medicine, San Francisco, addressed the Portland Academy of Medicine on January 11th, on "Antirheumatic Remedies," and the Medical History Society of the University of Oregon Medical School on January 12th, on "The One Hundred and Twenty-Fifth Anniversary of the Discovery of Morphine by Sertürner."

Ray Lyman Wilbur, Secretary of the Interior, addressed the New York Health Conference at the Hotels Roosevelt and Biltmore, New York City, on March 14th and 15th. Other speakers were: Surgeon-General Hugh S. Cumming, Dr. William H. Welch, of the Johns Hopkins University and Dr. Shirley W. Wynne and Matthias Nicoll, Jr., City and State Health Commissioners, respectively. The conference was under the joint auspices of the United States Public Health Service, the State Department of Health, the City Department of Health, the State Medical Society, the Milbank Memorial Fund, the State Charities Aid Association and the Community Health Council of the Bellevue-Yorkville Health Demonstration.

Cambria-Somerset Retail Druggists' Association has arranged for a series of lectures at Johnstown, Pa., by Prof. C. Leonard O'Connell, of Pittsburgh College of Pharmacy. The lectures are given at the monthly dinners of the Association.

**Edgar F. Carswell,** Local Secretary of the Portland A. PH. A. Convention presented a resolution at the mid-winter meeting of the Maine Pharmaceutical Association, which was adopted, asking that the Department of Pharmacy at the University of Maine be reëstablished; the resolution also included a provision for the appointment of a committee by the President of the Association to submit the proposition to the trustees and other officials of the University. The department was discontinued at the time of the World War. The resolution states that the re-establishment of the department is necessary for the better protection of the public in order that trained men may be available to dispense drugs and medicines prescribed by trained medical men. Further, that the association would pledge its best efforts to support the movement and will work with the trustees of the University to assure the success of the department.

**Edward Swallow** contributes an interesting article on "The Hospital Pharmacist as He Will Be" to *The Messenger*. He is also inviting suggestions on a Flag for Pharmacy. A report of the Committee is to be made at the Rapid City meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION.

W. H. Cousins, Jr., son of **Walter H. Cousins,** of *Southern Pharmaceutical Journal*, has been elected president of his class (sophomore) at Southern Methodist University.

*Bulletin* No. 14 of the Department of Agriculture, State of Florida, deals with "Some Drug Plants in Florida," by Dr. B. V. Christensen, of the College of Pharmacy, of the University of Florida.

**Editor Kantrowitz** of the *Apotheker Zeitung* is nearing the 50th anniversary of his connection with that publication. He is undertaking, this year, to conduct another European tour which leaves New York City July 11th.

We are in receipt of a reprint from the *American Druggist* of an article by **Dr. John C. Krantz, Jr.** on "Will Science Find a Drug to Cure Diabetes?"—A report of what has been accomplished with insulin, synthalin and myrtillin.

**S. S. Dworkin,** chairman of the Price Standardization Committee of N. Y. State Pharmaceutical Association, is offering three prizes for best letters discussing "Prohibition and Pharmacy." The prizes are three copies of the "American Pharmaceutical Recipe Book." Mr. Dworkin may be addressed, 151 St. Ann's Ave., New York, N. Y.

We are in receipt of a reprint from the *Messenger of Theta Kappa Psi*, entitled "Diphtheria Infection of the Genital Tract,"

by **Henry J. Goeckel** and **Leah G. Goeckel.**

Our fellow member **I. H. Shurtleff** is approaching his 80th birthday, the March issue of *Patchwork* present three generations of the family; in lineage I. H., Frederick A. and Alvah W.

**Jacques F. Briceland,** of Iowa City, who by the membership given by the prize of Professor Cooper is a member of the AMERICAN PHARMACEUTICAL ASSOCIATION writes of his appreciation of the gift and the value of the JOURNAL.

The *Southern Pharmaceutical Journal* is explaining, by questions and answers, the new pharmacy law which will soon become effective.

*The Mask*, of Kappa Psi Pharmaceutical Fraternity, is giving most helpful assistance to the promotion of the Pharmacy Corps for the U. S. Army. Dr. A. R. Bliss, the editor, is not only giving this assistance, but personally in every other way possible. The Bill is printed in full. Many of the articles in the issue of *The Mask* referred to, deal with activities of the AMERICAN PHARMACEUTICAL ASSOCIATION. Editor Bliss is always ready to use his influence in the promotion of fraternity and pharmacy.

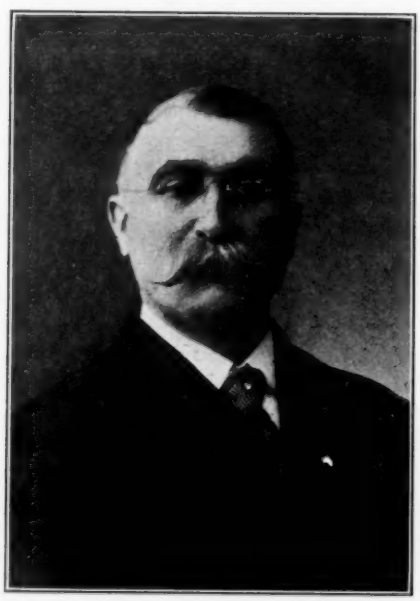
Die Gesellschaft für Geschichte der Pharmazie has issued another number of its periodical publications. As the others, this number is artistically illustrated; it gives the history of "F. Winkler's Stadtapotheke" in Innsbruck. This pharmacy has a family record of 350 years; the family tree is given and also brief accounts of the individual possessors. The illustrations show the furniture, apparatus, containers, etc., of various periods. The Society gives value received in return for its membership fees.

*Revista Filipina de Medicina Y Farmacia* has issued reprints of an article by Dr. Mariano D. del Rosario and Salud Garcia, on "Some Adulterants of Aspirin." The former has attended a meeting of the A. PH. A., and is head of the Philippine School of Pharmacy.

## OBITUARY.

### JOHN GRANVILLE GODDING.

Only a few weeks ago Mr. Godding advised us of the death of the Secretary of Massachusetts Pharmaceutical Association, Mr. Guerin, expressing his high regard for him and the loss of a dear friend by his death. Now we are called upon to record the passing of our esteemed co-worker and friend of many years; one who was ever ready to speak a good word and to commend; free from guile, he spoke evil of no one and never failed in an opportunity for a kindly word.



J. G. GODDING, BOSTON, MASS.
Pres. A. PH. A., 1910.

Mr. Godding was born 76 years ago in Gardiner, Maine, the son of Nathaniel and Rachel H. Godding. He received his early education in the schools of Gardiner and Brandon, Vt. As a youth he entered the drug business in the store of an uncle in Brandon and later engaged with A. W. Higgins in Rutland. Coming to Boston in 1871, he secured employment with Edward S. Kelley, owner of one of the leading pharmacies of Boston. He matriculated at the Massachusetts College of Pharmacy and received his diploma from that institution in 1874.

A friendship with the late S. A. D. Sheppard was established at this time, which continued until the death of the latter. Mr. Sheppard had been a member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1865, and induced his young friend to affiliate, when the ASSOCIATION met in Boston.

Mr. Godding secured employment with Henry A. Borell, Philadelphia, in 1875, but after two years he returned to Boston and engaged with Levi Tower, with whom he later formed a partnership and opened a pharmacy in the then new Back Bay district of Boston, at the corner of Dartmouth and Newbury streets. Mr. Tower retired in 1894 and Mr. Godding continued the pharmacy at the same location. Few, if any, pharmacists of Boston have been more highly regarded by the professions and laity.

On the 50th anniversary of his graduation, as an appreciation of his ability and his long and helpful service, the Massachusetts College of Pharmacy conferred the honorary degree of Doctor of Pharmacy on Mr. Godding. He became a member of the College in 1881 and was elected to the Board of Trustees in 1886; since 1890 he has been its treasurer.

A sketch of the former President appears in the May JOURNAL for 1925. As stated, he became a member of the ASSOCIATION in 1875 and has attended the greater number of the meetings since then. Usually, if not invariably, he was accompanied by Mrs. Godding, who is also a member of the ASSOCIATION and was Chairman of the Women's Section of the A. PH. A. for several years. For a number of terms Mr. Godding was member and officer of the Council A. PH. A. and served for a year as Chairman of the Section on Historical Pharmacy. In 1912–1913 he was President of the ASSOCIATION. Mr. Godding had been a member of the Massachusetts State Pharmaceutical Association since its organization; a member of the Boston Druggists' Association, the Boston Association of Retail Druggists and of the N. A. R. D. In all of the ASSOCIATION activities he has been supported by Mrs. Godding.

Mr. and Mrs. Godding (née Adelaide M. Smith, of Epping, N. H.) were married in 1880. Both have been active in church work and contributed largely to the beautiful church edifice of Newton, near their home, where the funeral services for the deceased were held on April 10th. The following were named as members of a Committee representing the AMERICAN PHARMACEUTICAL ASSOCIATION: C. H. Packard, Theodore J. Bradley, James F. Finneran, Wm. H. Glover, I. H. Shurtleff.

Mr. Godding was a member of the Boston Chamber of Commerce, Middlesex Club, a number of social organizations and the Masonic bodies, in several of which he had held official positions.

The sadness of Mr. Godding's death is greater because it was due to an accident, April 7th, which changed a home of happiness to one of deepest sorrow for the one who had shared the cares and joys with her devoted husband. Mr. Godding was awakened by gas fumes from the heater; going to the basement to investigate the cause he was overcome, and died before help could be given; Mrs. Godding, who awakened after her husband had gone downstairs, also suffered from the effects of the gas which had entered the upper floors. She was rushed to the hospital in time to save her life and word has reached us that she is recovering.

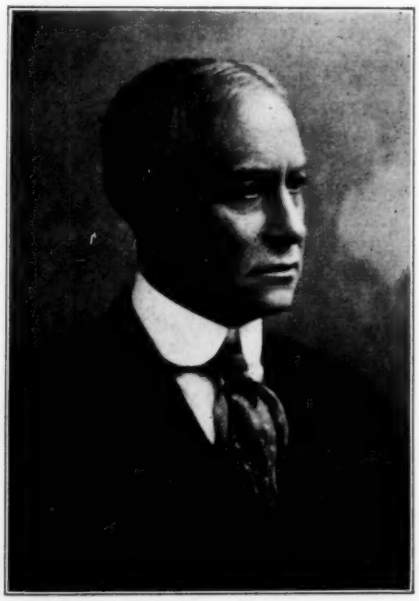
We repeat what another said of the deceased several years ago and it applies to all of his relations in life's activities:

"In his service to pharmaceutical organizations, he thinks only of the good of the cause and asks nothing for himself."

Heartfelt sympathy is extended to her whose sorrows are overflowing, and the hope is expressed that Mrs. Godding may have sustaining strength in her bereavement.

## JAMES F. GUERIN.

James F. Guerin, secretary of Massachusetts State Pharmaceutical Association for thirty-



JAMES F. GUERIN.

five consecutive years, and member of the AMERICAN PHARMACEUTICAL ASSOCIATION for

more than thirty years, died March 13th at his home in Worcester, the city of his birth and his home during all the years of his life.

Mr. Guerin entered the drug business as a youth and, in later years, acquired the store in which he began his business career; two years ago he celebrated the 50th anniversary of his entrance into pharmacy, at 236 Front Street. Highly esteemed by fellow pharmacists and citizens generally of Worcester, he is mourned by a host of friends. Delegations from many local organizations of which the deceased was a member were present at the services in St. Bernards Church; among them were representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION, the National Association of Retail Druggists. The Massachusetts State Pharmaceutical Association was largely represented by members from various cities; all came to do honor to one who had faithfully served in pharmacy, many mourned a friend whom they had known for many years. The Rev. F. Chester Leahy officiated at the requiem high mass.

Mr. Guerin was a former president of Division 3 A. O. H. and a member of A. O. H Building Corporation; honorary member of the Emmet Guards' Association; founder of the Washington Social Club; member of the original corporation of St. Vincent Hospital; for a number of years he was a member of the city school board, and held other positions of trust.

The deceased was born in Worcester, September 4, 1862. He is survived by his widow, Ellen F. (Fallon) Guerin; one son, Edmund L. and two daughters, Mary E. and Frances. William J., a son, died about a year ago.

Mr. Guerin kept abreast of the times and was a loyal supporter of the organizations of the drug trade, from local to national; he honored the office which he held for so many years. That his services were appreciated is testified to by the fact that his continuance in office was never questioned, and the realization of the great loss sustained by the ASSOCIATION.

**Dr. Frank S. Goodman,** Chief pharmacist of the U. S. Public Health Service, died at his home in Washington, D. C., February 22nd. He was trained in private schools of Annapolis, where he was born, in 1861; thereafter, he attended St. John's College and then graduated in medicine at Baltimore. He was appointed to the U. S. Public Health Service as a hospital steward in 1883, and had served continuously since that time at many Government hospitals and quarantine stations. In 1892 he contracted yellow fever in the line of duty and, being immune to the disease, performed valuable service in caring for patients during the epidemic at Dry Tortugas in 1894. From 1895 onward he served at many hospitals and quarantine stations, including Norfolk, Havana, Cuba, and other cities. In 1902 he was promoted to chief pharmacist. In 1923 he was transferred to the Bureau of the Public Health Service in Washington, where he remained on duty until his final illness. He is survived by his widow, and a son, Stanton Goodman, of Frederick, Md.

Hon. Thomas Taggart—who contributed largely to the entertainment of the AMERICAN PHARMACEUTICAL ASSOCIATION and other organizations of the drug trade when meeting in Indiana—died March 6th. As is generally known, the deceased was a power in politics for many years; he made friends and was loyal to them; nothing seemed to please him more than the opportunity of entertaining his friends and patrons. The widow, four daughters and a son survive the deceased. Mr. Taggart was born in Monyhon, Ireland in 1856.

**Joseph Collett Smith,** secretary of the Wellcome Foundation Limited and Manager of the Estates Department of Burroughs, Wellcome Co., London, Eng., died March 18th, aged 64 years.

Mr. Smith joined the staff of Burroughs, Wellcome & Co., in a junior capacity, in 1881. During his long and distinguished career, which extended to nearly a half century, he advanced through a series of positions to become secretary of the Wellcome Foundation Limited, a Director of some of its associated companies and Manager of the Estates Department of Burroughs, Wellcome & Co.

Mr. Smith is survived by his widow, son and daughter. Representative members of the staffs of Burroughs, Wellcome & Co., London, and of the associated scientific institutions were present at the funeral services on March 21st.

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The Federal Narcotic Board, comprised of the Secretaries of State, Treasury and Commerce, has decreased the amount of opium that can be legally imported into the United States during 1929 to 135,790 pounds, a decrease of 8 per cent over last year; the imports of coca leaves have been fixed at 176,000 pounds, a decrease of 25 per cent.

# LEGAL AND LEGISLATIVE.

## STATE LEGISLATION.

**Arizona** has enacted Senate Bill 22 regulating the distribution and sale of caustic and corrosive acids and alkalies.

**Arkansas** has enacted Senate Bill 241 defining portions of the pharmacy law and regulating the sale of drugs and poisons.

**Indiana** has enacted House Bill 177 requiring three years' pharmacy experience and eighteen months' schooling for registered assistant pharmacists.

The following bills have passed the **Colorado** House: Bill No. 35, amending the present act for the registration of pharmacists by requiring of the applicant three years in a college of pharmacy and two years of practical experience; House Bill 36, requiring a licensed pharmacist in each drug store; No. 37, allowing certain persons, in towns under 500 not having a licensed pharmacist, to sell drugs, medicines, and poisons compounded by a licensed pharmacist.

**Iowa** House Bill 96 provides for the suspension of the license of physicians and pharmacists who have been convicted of a violation of the federal statutes and regulations relating to intoxicating liquors or to narcotics.

**Kansas** has been successful in passing a pharmacy law with graduation prerequisites and in amending the drug act prohibiting the sale of coca and narcotics by providing that the provisions of the act shall not apply to decocainized coca leaves or preparations made therefrom or other preparations of coca leaves which do not contain cocaine.

The **Maryland** Legislature passed an amended bill regulating the sale and labeling of caustic acids and alkalies.

**Massachusetts** House Bill 59 authorizes the Department of Public Health to gather and disseminate public health information.

**Montana** House Bill 44 regulates the production, dispensing and possession of marihuana. House Bill 43 amends the state narcotic act by excluding marihuana from the list of drugs deemed to be narcotic.

**New Mexico** now has a law providing for instructions in the public schools on the effects of alcoholics and narcotics. House Bill 254 makes it unlawful to import, plant, cultivate, grow or possess or to barter, sell or distribute any cannabis indica and provides that cannabis indica may be imported for medicinal purposes only by licensed pharmacists and physicians.

Dr. Jacob Diner advises that no legislation affecting pharmacy was passed during this legislative session by the **New York** legislature.

**North Carolina** Senate Bill 41 permits druggists to fill alcoholic prescriptions written by physicians for medical purposes, in compliance with the provisions of the Volstead Act. Substitute for House Bill 222 would require the public schools of the state to furnish adequate instruction in the subject of alcoholism and narcotism. Senate Bill 277 provides for the license tax on the sale of drugs, medicines, alcohol and cosmetics.

**North Dakota** has amended the pharmacy license law by requiring at least two years of practical experience in a retail pharmacy by candidates for registration.

House Bill No. 413 of the **Ohio** Legislature seeks to amend the pharmacy law by adding to the list of drugs to which the act does not apply: aspirin tablets in original packages, powdered boric acid, camphorated oil, oil of cloves, carbolated petrolatum, Seidlitz powders and essence of peppermint.

Senate Bill No. 505 of the **Pennsylvania** Legislature seeks to prohibit the compounding, dispensing and preparation of drugs, medicines and poisons except by duly registered pharmacists or assistant pharmacists and charges the State Board of Pharmacy with the duty of enforcing the law.

Senate Bill 77 of the **South Dakota** Legislature amends the law relating to the State Board of Pharmacy by defining a pharmacopœia as the latest edition of the U. S. Pharmacopœia and the National Formulary as the latest edition of that work published by the AMERICAN PHARMACEUTICAL ASSOCIATION. Senate Bill 58 amends the law regulating the sale of poisons by scheduling under A and B drugs deemed to be poisons.

**Texas** will celebrate its Golden Anniversary association meeting with a new pharmacy law containing the prerequisite of graduation requirement of candidates for licenses.

In **Utah,** House Bill 157 provides for instruction in the public schools in physiology and hygiene with special reference to the injurious effects of alcoholics and narcotics on the human system and further provides that one hour per week shall be given to such instruction.

**Wyoming** Senate Bill 16 makes it unlawful to possess or distribute by any means whatever *Lophophora williamsii* (peyote) and *Agave americana* (maguey).

## BILLS IN CONGRESS.

Senate Joint Resolution 209, introduced by Senator Wheeler, Montana, creates a joint committee to be known as the Committee on Narcotic Traffic to make a study of the use of habit-forming drugs and to report not later than December 31, 1929, to the first session of the Seventy-First Congress, its findings and recommendations for the amendment and revision of existing laws necessary to prevent and curtail the unlawful sale, traffic and use of such drugs. The companion resolution in the House is H. J. Res. 404, introduced by Representative LaGuardia, New York.

H. R. 17058, introduced by Representative Wainwright, New York, proposes to increase the efficiency of the medical department of the regular army. The bill increases the number of medical, dental and veterinary personnel, both officers and enlisted men. Pharmacists are given little consideration in the Bill.

## CAMPHORATED OIL NOT A PATENT.

The appellant, Abramoff, appealed to the supreme court of New Jersey from a judgment entered by the district court in favor of the Board of Pharmacy of the State of New Jersey, in a penal action for an alleged violation of the Pharmacy Act. He, a grocer or ordinary tradesman, undertook to sell a small bottle of camphorated oil, corked and sealed, and bearing the imprint of a legally licensed pharmacist. On appeal, he argued among other things that Section 9 of the Pharmacy Act provides that everything therein shall be construed to cover the making and vending of non-poisonous patent or proprietary medicines. But, said the court, camphorated oil is neither a patent medicine nor a proprietary medicine. Consequently, a complete case of a violation of the act, not within the exceptions embodied in Section 9, was made out. The appeal was therefore dismissed.—*Jour. A. M. A.*

## AMENDMENT TO THE NEW JERSEY PHARMACY LAW.

On March 25, 1929, Governor Morgan F. Larson signed Senate Bill No. 17, amending the Pharmacy Law of the State of New Jersey which had passed the Senate on February 25, 1929 by a vote of 13 to 0 and the House of Assembly on March 18, 1929 by a vote of 48 to 0. This ammendment is now Chapter 15 of the Laws of 1929, and became effective the day it was signed. It provides that the examination fees for Registered Pharmacists and Assistant Pharmacists shall be $25.00 instead of the previous fee of $10.00. The ammendment also provides that every Registered Pharmacist and Assistant Pharmacist shall renew his registration annually instead of biennially, as heretofore required, and the re-registration fee is $2.00 annually in place of $1.00 biennially.

The amendment further provides that applicants for the Assistant Pharmacist Certificate must have successfully completed at least two years in a School of Pharmacy complying with the rules and regulations of the Board of Pharmacy of this state.

This amendment had the support of the New Jersey Pharmaceutical Association, the various local associations throughout the state, and of the Board of Pharmacy. The Legislative Committee of the New Jersey Pharmaceutical Association which sponsored the amendment, includes the following: Henry D. Kehr, Chairman, Trenton, N. J.; Samuel Lavigne, Newark, N. J.; Charles H. Jackson, Ventnor City, N. J.; John J. Debus, Jersey City, N. J.; James V. McFadden, Camden, N. J.; Louis C. Arnold, South Orange, N. J.; Robert P. Fischelis, Trenton, N. J.—R. P. Fischelis.

## DETERMINATION OF CHLOROFORM IN CHLOROFORM LINIMENT.

Edward M. Givens of Freehold, N. J., has favored us with the following method for determining the amount of chloroform in chloroform liniment. The method follows:

Into a resistance flask, using a high side-tube connection and a well-cooled condenser, mix 10 cc. of the sample and the same volume of sodium chloride solution *N*/5.

Slowly distil from 8 to 10 cc. of the mixture into a graduated receiver containing 10 cc. of 10% sulphuric acid. Add more of the acid if required to precipitate all the chloroform; agitate, and let stand until separation is complete and read the volume at the line of demarcation—that times 10 equals the per cent of chloroform present. The reporter states that the time required for making an assay is about 15 minutes, and that he has made several hundred of them.

The method was submitted to a referee who states that the use of sodium chloride in the distillation flask is clever. The only criticism he has to offer is that the amount of the sample to be distilled is too small. He suggests that 25 cc. of the chloroform liniment and a like amount of the salt solution should be used, and 35 cc. of the distillate should be collected in a casein tube or similar type tube so that the chloroformic layer may be centrifuged.

## BOOK NOTICES AND REVIEWS.

*Schmelzpunkttabelle der organischen Verbindungen*—"Table of Melting Points of Organic Compounds." By ASAHINA, NAKAO, TSUKAMOTO AND NAKHASHI; Publishers, Nakodo, Tokyo and Kioto, Japan. 220 pages. Price 5 yen, 1928.

This reference book is intended for pharmacists, chemists and biologists. It contains 5808 organic compounds, arranged according to their melting points, ranging from 10° to 419° C. Each compound has five columns: (1) Melting Point, (2) Remarks, (3) Name, (4) Formula and (5) Literature. Under "Remarks," the boiling points of the compounds are often given. The "Literature" is limited to 6 standard textbooks. In each page the limit of melting points of the compounds contained in that page appears on the top, and the page number at the bottom. The book can be used not only by the Orientals but also by the Occidentals, since the preface only is in Japanese. The text is in German, but understandable to a chemist of any nationality. The index of compounds at the end of the book, covering 46 pages, is also a helpful feature. The book is similar to "Kempf's Organische Verbindungen nach Schmelzpunkten," published by Friedr. Vieweg and Son, Braunschweig, Germany.—K. K. C.

*Pharmazeutische Synonyma*, Brieger. Compiled by DR. RICHARD BRIEGER, Science Editor of the *Pharmazeutische Zeitung*. Published by Julius Springer, Linkstrasse, 23–24, Berlin, Germany. Price R. M. 16.

Dr. Brieger has rendered a distinct service by the publication of this book; however, the foundation laid lends itself to enlargement in succeeding editions. Recently the writer was asked for the composition of "Nine Oils," referred to by Dickens and what is meant by "black stone," said to be used as a remedial agent in the United States. The former was known to the writer under other names; there is a question relative to what is meant by the latter term. We do not find "madstone" given in the book being reviewed. The late Dr. A. B. Lyons compiled almost a complete list of plant names, and Dr. Brieger, as stated, has laid a valuable foundation, which lends itself to enlargement, as the author states, in substance, in the *foreword*. He has attempted to give, and has succeeded in a large degree in giving to pharmacists a book that serves a useful purpose. The list of German synonyms is more complete than those of the other languages—English, French, Italian, Spanish and Dutch. Difficulties obtain in preparing a book of this kind and the author cites several examples, only one of them will be referred to, *Unguentum Hydrargyri album;* synonyms—"Ungentum Werhofii," "U. Werlhofii," "U. Walhofii." Possibly by search the origin may be discovered, but the author has placed limitations on his work, seeking to give the pharmacist the synonyms as he has found them, without going into the history. Page 2 gives 122 names and there are 276 pages in the book; possibly the number of items does not represent an average page, but if 100 is a better average then the titles listed would exceed 27,000.

Most every pharmacist who has practiced his profession for a decennium or two would have, at some time or other, given the price of the book to know the definition of an unfamiliar synonym.

*Actions and Uses of the Salicylates and Cinchophen.* By PROF. P. J. HANZLIK, Stanford University School of Medicine, Department of Pharmacology. The Williams & Wilkins Company, publishers. Price $3.50. 6 x 9. 184 pages, cloth.

The book named presents not only a review, but considers the pharmacological actions of the drugs indicated by the title. At the very outset the reviewer is impressed with the thoroughness of the author; the extent of the study is indicated by 658 references used in the text and about 100 others not used, which make the bibliography quite complete.

The subject matter is presented in 21 chapters; all of them have interest and value for the pharmacist; the second considers chemical and physical properties and it is indeed remarkable to have so much information on the subject in condensed form. The chapter on pharmacology and that on clinical reports are comprehensive records of studies and the many references concern particularly the physician and laboratorian; pharmacists will find the closing chapters, relating to toxicology, dosage and methods of administration very helpful in their practice. The monograph is deserving of commendation and a place in the pharmacist's library; the publishers have given deserved attention to the preparation of a volume by a painstaking research worker.